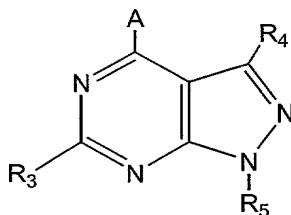


CLAIMS

The invention that is claimed is:

5 1. A pharmaceutical composition comprising a corticotropin releasing factor antagonist and a growth hormone secretagogue or growth hormone.

2. A pharmaceutical composition according to claim 1 wherein said corticotropin releasing factor antagonist is a compound of formula



10

or a pharmaceutically acceptable acid addition salt thereof, wherein

A is NR_1R_2 , $\text{CR}_1\text{R}_2\text{R}_{11}$, or $\text{C}(=\text{CR}_1\text{R}_{12})\text{R}_2$, $\text{NHCR}_1\text{R}_2\text{R}_{11}$, $\text{OCR}_1\text{R}_2\text{R}_{11}$, $\text{SCR}_1\text{R}_2\text{R}_{11}$, NHNHR_1R_2 , $\text{CR}_2\text{R}_{11}\text{NHR}_1$, $\text{CR}_2\text{R}_{11}\text{OR}_1$, $\text{CR}_2\text{R}_{11}\text{SR}_1$ or $\text{C}(\text{O})\text{R}_2$;

15 R_1 is hydrogen, or $\text{C}_1\text{-C}_6$ alkyl which may be substituted by one or two substituents R_6 independently selected from the group consisting of hydroxy, fluoro, chloro, bromo, iodo, $\text{C}_1\text{-C}_6$ alkoxy, $\text{O-C}(\text{O})\text{-(C}_1\text{-C}_6\text{ alkyl)}$, $\text{O-C}(\text{O})\text{-N}(\text{C}_1\text{-C}_4\text{ alkyl})(\text{C}_1\text{-C}_2\text{ alkyl})$; amino, $\text{NH}(\text{C}_1\text{-C}_4\text{ alkyl})$, $\text{S}(\text{C}_1\text{-C}_6\text{ alkyl})$, $\text{OC}(\text{O})\text{NH}(\text{C}_1\text{-C}_4\text{ alkyl})$, $\text{N}(\text{C}_1\text{-C}_2\text{ alkyl})\text{C}(\text{O})(\text{C}_1\text{-C}_4\text{ alkyl})$, $\text{NHC}(\text{O})(\text{C}_1\text{-C}_4\text{ alkyl})$, COOH , $\text{CO}(\text{C}_1\text{-C}_4\text{ alkyl})$, $\text{C}(\text{O})\text{NH}(\text{C}_1\text{-C}_4\text{ alkyl})$, $\text{C}(\text{O})\text{N}(\text{C}_1\text{-C}_4\text{ alkyl})(\text{C}_1\text{-C}_2\text{ alkyl})$, SH , CN , NO_2 , $\text{SO}(\text{C}_1\text{-C}_4\text{ alkyl})$; $\text{SO}_2(\text{C}_1\text{-C}_4\text{ alkyl})$, $\text{SO}_2\text{NH}(\text{C}_1\text{-C}_4\text{ alkyl})$, $\text{SO}_2\text{N}(\text{C}_1\text{-C}_4\text{ alkyl})(\text{C}_1\text{-C}_2\text{ alkyl})$, and said $\text{C}_1\text{-C}_6$ alkyl may have one or two double or triple bonds;

25 R_2 is $\text{C}_1\text{-C}_{12}$ alkyl, aryl or $(\text{C}_1\text{-C}_{10}\text{ alkylene})\text{aryl}$ wherein said aryl is phenyl, naphthyl, thienyl, benzothienyl, pyridyl, quinolyl, pyrazinyl, pyrimidyl, imidazolyl, furanyl, benzofuranyl, benzothiazolyl, isothiazolyl, benzisothiazolyl, thiazolyl, isoxazolyl, benzisoxazolyl, benzimidazolyl, triazolyl, pyrazolyl, pyrrolyl, indolyl, azaindolyl, oxazolyl, or benzoxazolyl; 3- to 8-membered cycloalkyl or $(\text{C}_1\text{-C}_6\text{ alkylene})\text{cycloalkyl}$, wherein said cycloalkyl may have one or two of O, S or N-Z, wherein Z is hydrogen, substituted, independently, for one or two carbons of said cycloalkyl, $\text{C}_1\text{-C}_4$ alkyl, benzyl or $\text{C}_1\text{-C}_4$ alkanoyl, wherein R^2 may be substituted independently by 30 from one to three of chloro, fluoro, or $\text{C}_1\text{-C}_4$ alkyl, or one of hydroxy, bromo, iodo, $\text{C}_1\text{-}$

C₆ alkoxy, OC(O)(C₁-C₆ alkyl), O-C-N(C₁-C₄ alkyl)(C₁-C₂ alkyl), S(C₁-C₆ alkyl), NH₂, NH(C₁-C₂ alkyl), N(C₁-C₄ alkyl) C(O)(C₁-C₄ alkyl), NHC(O)(C₁-C₄ alkyl), COOH, C(O)O(C₁-C₄ alkyl), C(O)NH(C₁-C₄ alkyl), C(O)N(C₁-C₄ alkyl)(C₁-C₂ alkyl), SH, CN, NO₂, SO(C₁-C₄ alkyl), SO₂(C₁-C₄ alkyl), SO₂NH(C₁-C₄ alkyl), SO₂N(C₁-C₄ alkyl)(C₁-C₂ alkyl), and wherein said C₁-C₁₂ alkyl or C₁-C₁₀ alkylene may have one to three double or triple bonds; or

NR₁R₂ or CR₁R₂R₁₁ may form a 4- to 8-membered ring optionally having one or two double bonds or one or two of O, S or N-Z wherein Z is hydrogen, C₁-C₄ alkyl, benzyl, or C₁-C₄ alkanoyl;

10 R₃ is hydrogen, C₁-C₆ alkyl, fluoro, chloro, bromo, iodo, hydroxy, amino, O(C₁-C₆ alkyl), NH(C₁-C₆ alkyl), N(C₁-C₄ alkyl)(C₁-C₂ alkyl), SH, S(C₁-C₄ alkyl), SO(C₁-C₄ alkyl), or SO₂(C₁-C₄ alkyl), wherein said C₁-C₄ alkyl and C₁-C₆ alkyl may have one or two double or triple bonds and may be substituted by from 1 to 3 R₇ substituents independently selected from the group consisting of hydroxy, amino, C₁-C₃ alkoxy, 15 dimethylamino, diethylamino, methylamino, ethylamino, NHC(O)CH₃, fluoro, chloro or C₁-C₃ thioalkyl;

R₄ is hydrogen, C₁-C₆ alkyl, fluoro, chloro, bromo, iodo, C₁-C₆ alkoxy, amino, NH(C₁-C₆ alkyl), N(C₁-C₆ alkyl) (C₁-C₂ alkyl), SO_n(C₁-C₆ alkyl), wherein n is 0, 1 or 2, cyano, hydroxy, carboxy, or amido, wherein said C₁-C₆ alkyls may be substituted by 20 one to three of hydroxy, amino, carboxy, amido, NHC(O)(C₁-C₄ alkyl), NH(C₁-C₄ alkyl), N(C₁-C₄ alkyl)(C₁-C₂ alkyl), C(O)O(C₁-C₄ alkyl), C₁-C₃ alkoxy, C₁-C₃ thioalkyl, fluoro, bromo, chloro, iodo, cyano or nitro;

R₅ is phenyl, naphthyl, thienyl, benzothienyl, pyridyl, quinolyl, pyrazinyl, pyrimidyl, imidazolyl, furanyl, benzofuranyl, benzothiazolyl, isothiazolyl, 25 benzoisothiazolyl, thiazolyl, isoxazolyl, benzisoxazolyl, benzimidazolyl, triazolyl, pyrazolyl, pyrrolyl, indolyl, pyrrolopyridyl benzoxazolyl, oxazolyl, pyrrolidinyl, thiazolidinyl, piperazinyl, piperidinyl, or tetrazolyl, wherein each one of the above groups may be substituted independently by from one to three of fluoro, chloro, bromo, formyl, C₁-C₆ alkyl, C₁-C₆ alkoxy or trifluoromethyl, or one of hydroxy, iodo, 30 cyano, nitro, amino, cyclopropyl, NH(C₁-C₄ alkyl), N(C₁-C₄ alkyl)(C₁-C₂ alkyl), COO(C₁-C₄ alkyl), CO(C₁-C₄ alkyl), SO₂NH(C₁-C₄ alkyl), SO₂N(C₁-C₄ alkyl)(C₁-C₂ alkyl), SO₂NH₂, NHSO₂(C₁-C₄ alkyl), S(C₁-C₆ alkyl), SO₂(C₁-C₆ alkyl), wherein said C₁-C₄ alkyl and C₁-C₆ alkyl may have one double or triple bond and may be

substituted by one or two of fluoro, chloro, hydroxy, amino, methylamino, dimethylamino or acetyl; with the proviso that R₅ is not unsubstituted phenyl;

R₁₁ is hydrogen, hydroxy, fluoro, chloro, COO(C₁-C₂ alkyl), cyano, or CO(C₁-C₂ alkyl); and

5 R₁₂ is hydrogen or C₁-C₄ alkyl;

with the provisos that:

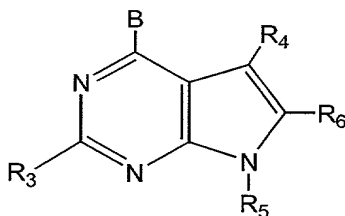
(a) A is not straight chain C₁-C₁₂ alkyl;

(b) when R₃ is hydrogen, A is benzyl or phenethyl, and R₄ is fluoro, chloro, bromo or iodo, then R₅ is not 5'-deoxy-ribofuranosyl or 5'-amino-5'-deoxy-

10 ribofuranosyl; and

(c) when R⁵ is phenyl, said phenyl is substituted by two or three substituents.

3. A pharmaceutical composition according to claim 1 wherein said
15 corticotropin releasing factor antagonist is a compound of formula



and the pharmaceutically acceptable acid addition salts thereof, wherein

B is NR₁R₂, CR₁R₂R₁₁, C(=CR₂R₁₂)R₁, NHR₁R₂R₁₁, OCR₁R₂R₁₁, SCR₁R₂R₁₁, NHNR₁R₂, CR₂R₁₁NHR₁, CR₂R₁₁OR₁, CR₂R₁₁SR₁, or C(O)R₂;

20 R₁ is hydrogen, or C₁-C₆ alkyl which may be substituted by one or two substituents R₇ independently selected from the group consisting of hydroxy, fluoro, chloro, bromo, iodo, C₁-C₈ alkoxy, O-C(=O)-(C₁-C₆ alkyl), O-C(=O)NH(C₁-C₄ alkyl), O-C(=O)-N(C₁-C₄ alkyl)(C₁-C₂ alkyl), amino, NH(C₁-C₄ alkyl), N(C₁-C₂ alkyl)(C₁-C₄ alkyl), S(C₁-C₆ alkyl), N(C₁-C₄alkyl)C(=O)(C₁-C₄ alkyl), NH(C₁-C₄ alkyl), COOH, C(=O)O(C₁-
25 C₄ alkyl), C(=O)NH(C₁-C₄ alkyl), C(=O)N(C₁-C₄ alkyl)(C₁-C₂ alkyl), SH, CN, NO₂, SO(C₁-C₄ alkyl), SO₂(C₁-C₄ alkyl), SO₂NH(C₁-C₄ alkyl), SO₂N(C₁-C₄ alkyl)(C₁-C₂ alkyl), and said C₁-C₆ alkyl may contain one or two double or triple bonds;

R₂ is C₁-C₁₂ alkyl, aryl or (C₁-C₁₀ alkylene)aryl wherein said aryl is phenyl, naphthyl, thienyl, benzothienyl, pyridyl, quinolyl, pyrazinyl, pyrimidyl, imidazolyl,
30 furanyl, benzofuranyl, benzothiazolyl, isothiazolyl, benzisothiazolyl, thiazolyl,

- isoxazolyl, benzisoxazolyl, benzimidazolyl, triazolyl, pyrazolyl, pyrrolyl, indolyl, pyrrolopyridyl, oxazolyl, or benzoxazolyl; 3- to 8-membered cycloalkyl or (C₁-C₆ alkylene) cycloalkyl, wherein said cycloalkyl may contain one or two of O, S or N-Z wherein Z is hydrogen, C₁-C₄ alkyl, benzyl or C₁-C₄ alkanoyl, wherein R₂ may be
- 5 substituted independently by from one to three of chloro, fluoro, or C₁-C₄ alkyl, or one of hydroxy, bromo, iodo, C₁-C₆ alkoxy, O-C(=O)-(C₁-C₆ alkyl), O-C-N(C₁-C₄ alkyl)(C₁-C₂ alkyl), S(C₁-C₆ alkyl), NH₂, NH(C₁-C₂ alkyl), N(C₁-C₂ alkyl) (C₁-C₄ alkyl), N(C₁-C₄)-C(=O)(C₁-C₄ alkyl), NHC(=O)(C₁-C₄), COOH, C(=O)O(C₁-C₄ alkyl), C(=O)NH(C₁-C₄ alkyl), C(=O)N(C₁-C₄ alkyl)(C₁-C₂ alkyl), SH, CN, NO₂, SO(C₁-C₄ alkyl), SO₂(C₁-C₄ alkyl), SO₂NH(C₁-C₄ alkyl), SO₂N(C₁-C₄ alkyl)(C₁-C₂ alkyl), and wherein said C₁-C₁₂ alkyl or C₁-C₁₀ alkylene may contain one to three double or triple bonds; or

NR₁R₂ or CR₁R₂R₁₁ may form a saturated 3- to 8 membered carbocyclic ring of which the 5- to 8-membered ring contain one or two double bonds or one or two of O, S or N-Z wherein Z is hydrogen, C₁-C₄ alkyl, benzyl or C₁-C₄ alkanoyl;

- 15 R₃ is hydrogen, C₁-C₆ alkyl, fluoro, chloro, bromo, iodo, hydroxy, amino, O(C₁-C₆ alkyl), NH(C₁-C₆ alkyl), N(C₁-C₄ alkyl)(C₁-C₂ alkyl), SH, S(C₁-C₄ alkyl), SO(C₁-C₄ alkyl), or SO₂(C₁-C₄ alkyl), wherein said C₁-C₄ alkyl and C₁-C₆ alkyl may contain from one or two double or triple bonds and may be substituted by from 1 to 3 substituents R₈ independently selected from the group consisting of hydroxy, amino, C₁-C₃ alkoxy, dimethylamino, diethylamino, methylamino, ethylamino, NHCH₃, fluoro, chloro or C₁-C₃ thioalkyl;
- 20

- R₄ and R₆ are each independently hydrogen, C₁-C₆ alkyl, fluoro, chloro, bromo, iodo, C₁-C₆ alkoxy, amino, NH(C₁-C₆ alkyl), N(C₁-C₆ alkyl)(C₁-C₂ alkyl), SO_n(C₁-C₆ alkyl), wherein n is 0, 1 or 2, cyano, hydroxy, carboxy, or amido, wherein
- 25 said C₁-C₆ alkyls may be substituted by one to three of hydroxy, amino, carboxy, amido, NHC(=O)(C₁-C₄ alkyl), NH(C₁-C₄ alkyl), N(C₁-C₄ alkyl)(C₁-C₂ alkyl), C(=O)O(C₁-C₄ alkyl), C₁-C₃ alkoxy, C₁-C₃ thioalkyl, fluoro, bromo, chloro, iodo, cyano or nitro;

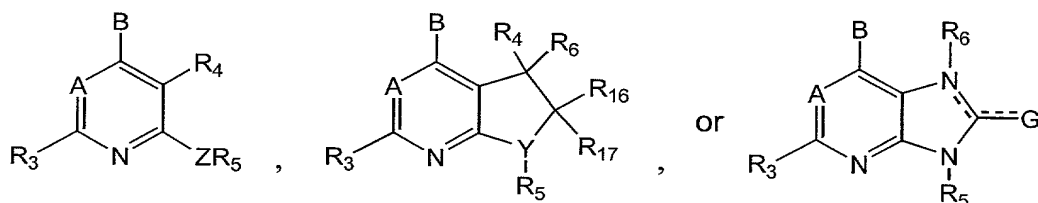
- R₅ is phenyl, naphthyl, thienyl, benzothienyl, pyridyl, quinolyl, pyrazinyl, pyrimidyl, imidazolyl, furanyl, benzofuranyl, benzothiazolyl, isothiazolyl, benzisothiazolyl, thiazolyl, isoxazolyl, benzisoxazolyl, benzimidazolyl, triazolyl, pyrazolyl, pyrrolyl, indolyl, azaindolyl, benzoxazolyl, oxazolyl, pyrrolidinyl, thiazolidinyl, morpholinyl, piperidinyl, piperazinyl, tetrazolyl, or 3- to 8-membered cycloalkyl or 9- to 12-membered bicycloalkyl, optionally containing one to three of O, S or N-Z wherein
- 30

Z is hydrogen, C₁-C₄ alkyl, C₁-C₄ alkanoyl, phenyl or phenylmethyl, wherein each one of the above groups may be substituted independently by from one to four of fluoro, chloro, C₁-C₆ alkyl, C₁-C₆ alkoxy or trifluoromethyl, or one of bromo, iodo, cyano, nitro, amino, NH(C₁-C₄ alkyl), N(C₁-C₄)(C₁-C₂ alkyl), COO(C₁-C₄ alkyl), CO(C₁-C₄ alkyl), SO₂NH(C₁-C₄ alkyl), SO₂N(C₁-C₄ alkyl)(C₁-C₂ alkyl), SO₂NH₂, NHSO₂(C₁-C₄ alkyl), S(C₁-C₆ alkyl), SO₂(C₁-C₆ alkyl), wherein said C₁-C₄ alkyl and C₁-C₆ alkyl may be substituted by one or two of fluoro, chloro, hydroxy, amino, methylamino, dimethylamino or acetyl; with the proviso that R₅ is not unsubstituted phenyl;

R₁₁ is hydrogen, hydroxy, fluoro, chloro, COO(C₁-C₂ alkyl), cyano, or CO(C₁-C₂ alkyl); and

R₁₂ is hydrogen or C₁-C₄ alkyl; with the proviso that (1) when R₅ is 4-bromophenyl, R₃ is hydrogen, and R₄ and R₆ are methyl, then B is not methylamino or ethyl, and (2) when R₅ is 4-bromophenyl, and R₃, R₄ and R₆ are methyl, then B is not 2-hydroxyethylamino.

4. A pharmaceutical composition according to claim 1 wherein said corticotropin releasing factor antagonist is a compound of formula



wherein

A is CR₇ or N;

B is NR₁R₂, CR₁R₂R₁₁, C(=CR₂R₁₂)R₁, NHCHR₁R₂, OCHR₁R₂, SCHR₁R₂, CHR₂OR₁₂, CHR₂SR₁₂, C(S)R₂ or C(O)R₂;

G is oxygen, sulfur, NH, NH₃, hydrogen, methoxy, ethoxy, trifluoromethoxy, methyl, ethyl, thiomethoxy, NH₂, NHCH₃, N(CH₃)₂ or trifluoromethyl;

Y is CH or N;

Z is NH, O, S, N (C₁-C₂ alkyl), or CR₁₃R₁₄, wherein R₁₃ and R₁₄ are each independently hydrogen, trifluoromethyl, or C₁-C₄ alkyl, or one of R₁₃ and R₁₄ may be cyano, chloro, bromo, iodo, fluoro, hydroxy, O(C₁-C₂ alkyl), amino, NH(C₁-C₂ alkyl), or CR₁₃R₁₄ may be C=O or cyclopropyl;

R_1 is C_1 - C_6 alkyl which may be substituted by one or two substituents R_8 independently selected from the group consisting of hydroxy, fluoro, chloro, bromo, iodo, C_1 - C_4 alkoxy, O - CO -(C_1 - C_4 alkyl), O - CO - NH (C_1 - C_4 alkyl), O - CO - N (C_1 - C_4 alkyl)(C_1 - C_2 alkyl), NH (C_1 - C_4 alkyl), N (C_1 - C_2 alkyl)(C_1 - C_4 alkyl), S (C_1 - C_4 alkyl), N (C_1 - C_4 alkyl) CO (C_1 - C_4 alkyl), $NHCO$ (C_1 - C_4 alkyl), COO (C_1 - C_4 alkyl), $CONH$ (C_1 - C_4 alkyl), CON (C_1 - C_4 alkyl)(C_1 - C_2 alkyl), S (C_1 - C_4 alkyl), CN , NO_2 , SO (C_1 - C_4 alkyl), SO_2 (C_1 - C_4 alkyl), and said C_1 - C_6 alkyl or C_1 - C_4 alkyl may contain one double or triple bond;

R_2 is C_1 - C_{12} alkyl, aryl or (C_1 - C_4 alkylene)aryl wherein said aryl is phenyl, naphthyl, thienyl, benzothienyl, pyridyl, quinolyl, pyrazinyl, pyrimidyl, imidazolyl, furanyl, benzofuranyl, benzothiazolyl, isothiazolyl, benzisothiazolyl, benzisoxazolyl, benzimidazolyl, indolyl, or benzoxazolyl; 3- to 8-membered cycloalkyl or (C_1 - C_6 alkylene)cycloalkyl, wherein said cycloalkyl may contain one or two of O , S or N - R_9 wherein R_9 is hydrogen, or C_1 - C_4 alkyl, wherein the above defined R_2 may be substituted independently by from one to three of chloro, fluoro, or C_1 - C_4 alkyl, or one of bromo, iodo, C_1 - C_6 alkoxy, O - CO -(C_1 - C_6 alkyl), O - CO - N (C_1 - C_4 alkyl)(C_1 - C_2 alkyl), S (C_1 - C_6 alkyl), CN , NO_2 , SO (C_1 - C_4 alkyl), or SO_2 (C_1 - C_4 alkyl), and wherein said C_1 - C_{12} alkyl or C_1 - C_4 alkylene may contain one double or triple bond; or

NR_1R_2 or $CR_1R_2R_{11}$ may form a saturated 5- to 8-membered carbocyclic ring which may contain one or two double bonds or one or two of O or S ;

R_3 is methyl, ethyl, fluoro, chloro, bromo, iodo, cyano, methoxy, OCF_3 , methylthio, methylsulfonyl, CH_2OH or CH_2OCH_3 ;

R_4 is hydrogen, C_1 - C_4 alkyl, fluoro, chloro, bromo, iodo, C_1 - C_4 alkoxy, amino, nitro, NH (C_1 - C_4 alkyl), N (C_1 - C_4 alkyl)(C_1 - C_2 alkyl), SO_n (C_1 - C_4 alkyl), wherein n is 0, 1 or 2, cyano, hydroxy, CO (C_1 - C_4 alkyl), CHO , or COO (C_1 - C_4 alkyl), wherein said C_1 - C_4 alkyl may contain one or two double or triple bonds and may be substituted by one or two of hydroxy, amino, carboxy, $NHCOCH_3$, NH (C_1 - C_2 alkyl), N (C_1 - C_2 alkyl) $_2$, COO (C_1 - C_4 alkyl), CO (C_1 - C_4 alkyl), C_1 - C_3 alkoxy, C_1 - C_3 thioalkyl, fluoro, chloro, cyano or nitro;

R_5 is phenyl, naphthyl, thienyl, benzothienyl, pyridyl, quinolyl, pyrazinyl, pyrimidyl, furanyl, benzofuranyl, benzothiazolyl, or indolyl, wherein each one of the above groups R_5 is substituted independently by from one to three of fluoro, chloro, C_1 - C_6 alkyl, or C_1 - C_6 alkoxy, or one of hydroxy, iodo, bromo, formyl, cyano, nitro, trifluoromethyl, amino, NH (C_1 - C_4 alkyl), N (C_1 - C_6)(C_1 - C_2 alkyl), $COOH$, COO (C_1 - C_4 alkyl), CO (C_1 - C_4 alkyl), SO_2NH (C_1 - C_4 alkyl), SO_2N (C_1 - C_4 alkyl)(C_1 - C_2 alkyl), SO_2NH_2 ,

NHSO₂(C₁-C₄ alkyl), S(C₁-C₆ alkyl), or SO₂(C₁-C₆ alkyl), wherein said C₁-C₄ alkyl and C₁-C₆ alkyl may be substituted by one or two of fluoro, hydroxy, amino, methylamino, dimethylamino or acetyl;

5 R₆ is hydrogen, or C₁-C₆ alkyl, wherein said C₁-C₆ alkyl may be substituted by one hydroxy, methoxy, ethoxy or fluoro;

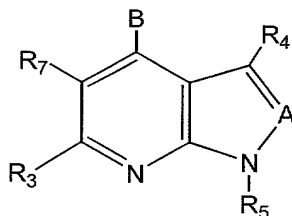
R₇ is hydrogen, C₁-C₄ alkyl, fluoro, chloro, bromo, iodo, cyano, hydroxy, O(C₁-C₄ alkyl), C(O)(C₁-C₄ alkyl), or C(O)O(C₁-C₄ alkyl), wherein the C₁-C₄ alkyl groups may be substituted with one hydroxy, chloro or bromo, or one to three fluoro;

R₁₁ is hydrogen, hydroxy, fluoro, or methoxy;

10 R₁₂ is hydrogen or C₁-C₄ alkyl; and

R₁₆ and R₁₇ are each independently hydrogen, hydroxy, methyl, ethyl, methoxy, or ethoxy, except that they are not both methoxy or ethoxy, and CR₄R₆ and CR₁₆R₁₇ each independently may be C=O.

15 5. A pharmaceutical composition according to claim 1 wherein said corticotropin releasing factor antagonist is a compound of formula



and the pharmaceutically acceptable acid addition salts thereof, wherein

A is N or -CR₆;

20 B is -NR₁R₂, -CR₁R₂R₁₁, -C(=CR₂R₁₂)R₁, -NHCHR₁R₂, -OCHR₁R₂, -SCHR₁R₂, -CHR₂OR₁₂, -CHR₂SR₁₂, -C(S)R₁ or -C(O)R₁;

R₁ is C₁-C₆ alkyl which may optionally be substituted with one or two substituents independently selected from the group consisting of hydroxy, fluoro, chloro, bromo, iodo, C₁-C₄ alkoxy, -O-CO-(C₁-C₄ alkyl), -O-CO-NH(C₁-C₄ alkyl), -O-CO-N(C₁-C₄ alkyl)(C₁-C₂ alkyl), -NH(C₁-C₄ alkyl), -N(C₁-C₂ alkyl)(C₁-C₄ alkyl), -S(C₁-C₄ alkyl), -N(C₁-C₄ alkyl)CO(C₁-C₄ alkyl), -NHCO(C₁-C₄ alkyl), -COO(C₁-C₄ alkyl), -CONH(C₁-C₄ alkyl), -CON(C₁-C₄ alkyl)(C₁-C₂ alkyl), CN, NO₂, -SO(C₁-C₄ alkyl), -SO₂(C₁-C₄ alkyl), and wherein any of the foregoing C₁-C₄ alkyl and C₁-C₆ alkyl groups may optionally contain one carbon-carbon double or triple bond;

- R_2 is C_1 - C_{12} alkyl, aryl, $-(C_1$ - C_4 alkylene)aryl wherein said aryl is phenyl, naphthyl, thienyl, benzothienyl, pyridyl, quinolyl, pyrazinyl, pyrimidyl, imidazolyl, furanyl, benzofuranyl, benzothiazolyl, isothiazolyl, benzisothiazolyl, thiazolyl, isoxazolyl, benzisoxazolyl, benzimidazolyl, triazolyl, pyrazolyl, pyrrolyl, indolyl,
- 5 oxazolyl, or benzoxazolyl; or 3- to 8- membered cycloalkyl or $-(C_1$ - C_6 alkylene)cycloalkyl, wherein one or two of the ring carbons of said cycloalkyl having at least 4 ring members and the cycloalkyl moiety of said $-(C_1$ - C_6 alkylene)cycloalkyl having at least 4 ring members may optionally be replaced by an oxygen or sulfur atom or by N-Z wherein Z is hydrogen; or C_1 - C_4 alkyl, and wherein each of said
- 10 groups R_2 may optionally be substituted with from one to three substituents independently selected from chloro, fluoro, and C_1 - C_4 alkyl, or by one substituent selected from bromo, iodo, C_1 - C_6 alkoxy, $-O-CO-(C_1$ - C_6 alkyl), $-S(C_1$ - C_6 alkyl), $-COO(C_1$ - C_4 alkyl), CN, NO_2 , $-SO(C_1$ - C_4 alkyl), and $-SO_2(C_1$ - C_4 alkyl), and wherein said C_1 - C_{12} alkyl and the C_1 - C_4 alkylene moiety of said $-(C_1$ - C_4 alkylene)aryl may
- 15 optionally contain one carbon-carbon double or triple bond;
- or $-NR_1R_2$ may form a saturated 5- to 8-membered heterocyclic ring, or $-CHR_1R_2$ may form a saturated 5- to 8-membered carbocyclic ring, wherein each of these rings may optionally contain one or two carbon-carbon double bonds and wherein one or two of the carbon atoms of each of these rings may optionally be
- 20 replaced with a sulfur or oxygen atom;
- R_3 is C_1 - C_4 alkyl, fluoro, chloro, bromo, iodo, $-CH_2OH$, $-CH_2OCH_3$, $-O(C_1$ - C_3 alkyl), $-S(C_1$ - C_3 alkyl), or $-SO_2(C_1$ - C_3 alkyl), wherein said C_1 - C_3 alkyl may optionally contain one carbon-carbon double or triple bond;
- R_4 is hydrogen, C_1 - C_6 alkyl, fluoro, chloro, bromo, iodo, C_1 - C_4 alkoxy, amino,
- 25 $-NHCH_3$, $-N(CH_3)_2$, $-CH_2OH$, $-CH_2OCH_3$, or $-SO_n(C_1$ - C_4 alkyl), wherein n is 0, 1 or 2, cyano, hydroxy, $-CO(C_1$ - C_4 alkyl), $-CHO$, or $-COO(C_1$ - C_4 alkyl) wherein the C_1 - C_4 alkyl moieties in the foregoing R_4 groups may optionally contain one carbon-carbon double or triple bond;
- R_5 is phenyl, naphthyl, thienyl, benzothienyl, pyridyl, pyrimidyl, benzofuranyl,
- 30 pyrazinyl or benzothiazolyl, wherein each one of said groups R_5 may optionally be substituted with from one to three substituents independently selected from fluoro, chloro, C_1 - C_6 alkyl and C_1 - C_6 alkoxy, or by one substituent selected from iodo, hydroxy, bromo, formyl, cyano, nitro, amino, trifluoromethyl, $-NH(C_1$ - C_4 alkyl), $-N(C_1$ - $C_6)(C_1$ - C_2 alkyl), $-COO(C_1$ - C_4 alkyl), $-CO(C_1$ - C_4 alkyl), $-COOH$, $-SO_2NH(C_1$ - C_4 alkyl),

-SO₂N(C₁-C₄ alkyl)(C₁-C₂ alkyl), -SO₂NH₂, -NHSO₂(C₁-C₄ alkyl), -S(C₁-C₆ alkyl) and -SO₂(C₁-C₆ alkyl), wherein each of said C₁-C₄ alkyl and C₁-C₆ alkyl moieties in the foregoing R⁵ groups may optionally be substituted with one to three fluorine atoms;

R₆ is hydrogen, C₁-C₄ alkyl, fluoro, chloro, bromo, iodo, -CH₂OH, -CH₂OCH₃,
5 or C₁-C₄ alkoxy;

R₇ is hydrogen, C₁-C₄ alkyl, fluoro, chloro, bromo, iodo, -O(C₁-C₄ alkyl), cyano, -CH₂OH, -CH₂O(C₁-C₂ alkyl), -CO(C₁-C₂ alkyl), or -COO(C₁-C₂ alkyl);

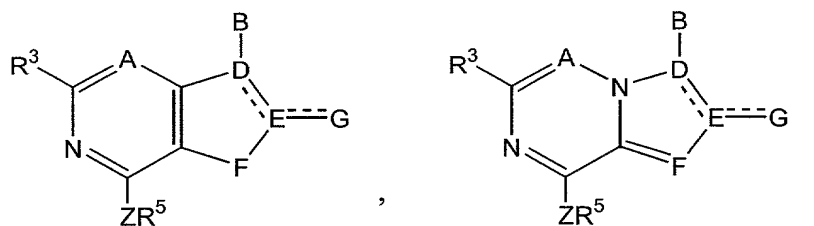
R₁₁ is hydrogen, hydroxy, fluoro, or methoxy; and

R₁₂ is hydrogen or C₁-C₄ alkyl;

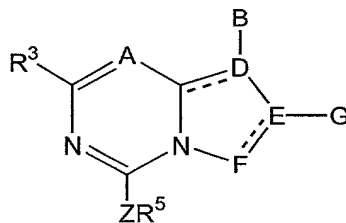
10 with the proviso that when A is N, then: (a) B is not unsubstituted alkyl; (b) R₅ is not unsubstituted phenyl or monosubstituted phenyl; and (c) R₃ is not unsubstituted alkyl;

or a pharmaceutically acceptable salt of such compound.

15 6. A pharmaceutical composition according to claim 1 wherein said corticotropin releasing factor antagonist is a compound of formula



or



or a pharmaceutically acceptable salt thereof, wherein

20 the dashed lines represent optional double bonds;

A is nitrogen or CR⁷;

B is -NR¹R², -CR¹R²R¹⁰, -C(=CR²R¹¹)R¹, -NHCR¹R²R¹⁰, -OCR¹R²R¹⁰, -SCR¹R²R¹⁰, -CR²R¹⁰NHR¹, -CR²R¹⁰OR¹, -CR²R¹⁰SR¹ or -COR²;

D is nitrogen and is single bonded to all atoms to which it is attached, or D is carbon and is either double bonded to E in formulas I and II or double bonded to the adjacent carbon atom common to both fused rings in formula III, or D is CH and is single bonded to E in formulas I and II;

5 E is nitrogen, CH or carbon;

F is oxygen, sulfur, CHR^4 or NR^4 when it is single bonded to E and F is nitrogen or CR^4 when it is double bonded to E;

10 G, when single bonded to E, is hydrogen, $\text{C}_1\text{-C}_4$ alkyl, $-\text{S}(\text{C}_1\text{-C}_4 \text{ alkyl})$, $-\text{O}(\text{C}_1\text{-C}_4 \text{ alkyl})$, NH_2 , $-\text{NH}(\text{C}_1\text{-C}_4 \text{ alkyl})$ or $-\text{N}(\text{C}_1\text{-C}_2 \text{ alkyl})(\text{C}_1\text{-C}_4 \text{ alkyl})$, wherein each of the $\text{C}_1\text{-C}_4$ alkyl groups of G may optionally be substituted with one hydroxy, $-\text{O}(\text{C}_1\text{-C}_2 \text{ alkyl})$ or fluoro group; G, when double bonded to E, is oxygen, sulfur or NH; and G, when E is nitrogen and double bonded to D or F, is absent;

15 R^1 is hydrogen, $\text{C}_1\text{-C}_6$ alkyl optionally substituted with one or two substituents R^8 independently selected from hydroxy, fluoro, chloro, bromo, iodo, $\text{C}_1\text{-C}_4$ alkoxy, CF_3 , $-\text{C}(=\text{O})\text{O}(\text{C}_1\text{-C}_4 \text{ alkyl})$, $-\text{OC}(=\text{O})(\text{C}_1\text{-C}_4 \text{ alkyl})$, $-\text{OC}(=\text{O})\text{N}(\text{C}_1\text{-C}_4 \text{ alkyl})(\text{C}_1\text{-C}_2 \text{ alkyl})$, $-\text{NHCO}(\text{C}_1\text{-C}_4 \text{ alkyl})$, $-\text{COOH}$, $-\text{COO}(\text{C}_1\text{-C}_4 \text{ alkyl})$, $-\text{CONH}(\text{C}_1\text{-C}_4 \text{ alkyl})$, $-\text{CON}(\text{C}_1\text{-C}_4 \text{ alkyl})(\text{C}_1\text{-C}_2 \text{ alkyl})$, $-\text{S}(\text{C}_1\text{-C}_4 \text{ alkyl})$, $-\text{CN}$, $-\text{NO}_2$, $-\text{SO}(\text{C}_1\text{-C}_4 \text{ alkyl})$, $-\text{SO}_2(\text{C}_1\text{-C}_4 \text{ alkyl})$, $-\text{SO}_2\text{NH}(\text{C}_1\text{-C}_4 \text{ alkyl})$ and $-\text{SO}_2\text{N}(\text{C}_1\text{-C}_4 \text{ alkyl})(\text{C}_1\text{-C}_2 \text{ alkyl})$, wherein each of the $\text{C}_1\text{-C}_4$ alkyl groups in the foregoing R^1 groups may optionally contain one or two double or
20 triple bonds;

25 R^2 is $\text{C}_1\text{-C}_{12}$ alkyl which may optionally contain from one to three double or triple bonds, aryl or $(\text{C}_1\text{-C}_4 \text{ alkylene})\text{aryl}$, wherein said aryl and the aryl moiety of said $(\text{C}_1\text{-C}_4 \text{ alkylene})\text{aryl}$ is selected from phenyl, naphthyl, thienyl, benzothienyl, pyridyl, quinolyl, pyrazinyl, pyrimidinyl, imidazolyl, furanyl, benzofuranyl, benzothiazolyl, isothiazolyl, pyrazolyl, pyrrolyl, indolyl, pyrrolopyridyl, oxazolyl and benzoxazolyl; $\text{C}_3\text{-C}_8$ cycloalkyl or $(\text{C}_1\text{-C}_6 \text{ alkylene})(\text{C}_3\text{-C}_8 \text{ cycloalkyl})$, wherein one or two of the carbon atoms of said cycloalkyl and the 5 to 8 membered cycloalkyl moieties of said $(\text{C}_1\text{-C}_6 \text{ alkylene})(\text{C}_3\text{-C}_8 \text{ cycloalkyl})$ may optionally and independently be replaced by an oxygen or sulfur atom or by NZ^2 wherein Z^2 is selected from hydrogen, $\text{C}_1\text{-C}_4$ alkyl, benzyl and $\text{C}_1\text{-C}_4$ alkanoyl, and wherein each of the foregoing R^2 groups may
30 optionally be substituted with from one to three substituents independently selected from chloro, fluoro, hydroxy and $\text{C}_1\text{-C}_4$ alkyl, or with one substituent selected from bromo, iodo, $\text{C}_1\text{-C}_6$ alkoxy, $-\text{OC}(=\text{O})(\text{C}_1\text{-C}_6 \text{ alkyl})$, $-\text{OC}(=\text{O})\text{N}(\text{C}_1\text{-C}_4 \text{ alkyl})(\text{C}_1\text{-C}_2 \text{ alkyl})$, $-\text{S}(\text{C}_1\text{-C}_6 \text{ alkyl})$, amino, $-\text{NH}(\text{C}_1\text{-C}_2 \text{ alkyl})$, $-\text{N}(\text{C}_1\text{-C}_2 \text{ alkyl})(\text{C}_1\text{-C}_4 \text{ alkyl})$, $-\text{N}(\text{C}_1\text{-C}_4 \text{ alkyl})$ -

CO-(C₁-C₄ alkyl), -NHCO(C₁-C₄ alkyl), -COOH, -COO(C₁-C₄ alkyl), -CONH(C₁-C₄ alkyl), -CON(C₁-C₄ alkyl)(C₁-C₂ alkyl), -SH, -CN, -NO₂, -SO(C₁-C₄ alkyl), -SO₂(C₁-C₄ alkyl), -SO₂NH(C₁-C₄ alkyl) and -SO₂N(C₁-C₄ alkyl)(C₁-C₂ alkyl);

-NR¹R² or CR¹R²R¹⁰ may form a saturated 3 to 8 membered carbocyclic ring

- 5 which may optionally contain from one to three double bonds and wherein one or two of the ring carbon atoms of such 5 to 8 membered rings may optionally and independently be replaced by an oxygen or sulfur atom or by NZ³ wherein Z³ is hydrogen, C₁-C₄ alkyl, benzyl or C₁-C₄ alkanoyl;

- R³ is hydrogen, C₁-C₄ alkyl, -O(C₁-C₄ alkyl), chloro, fluoro, bromo, iodo, -CN, 10 -S(C₁-C₄ alkyl) or -SO₂(C₁-C₄ alkyl) wherein each of the (C₁-C₄ alkyl) moieties in the foregoing R³ groups may optionally be substituted with one substituent R⁹ selected from hydroxy, fluoro and (C₁-C₂ alkoxy);

- each R⁴ is, independently, hydrogen, (C₁-C₆ alkyl), fluoro, chloro, bromo, iodo, hydroxy, cyano, amino, nitro, -O(C₁-C₄ alkyl), -N(C₁-C₄ alkyl)(C₁-C₂ alkyl), -S(C₁-C₄ 15 alkyl), -SO(C₁-C₄ alkyl), -SO₂(C₁-C₄ alkyl), -CO(C₁-C₄ alkyl), -C(=O)H or -C(=O)O(C₁-C₄ alkyl), wherein each of the (C₁-C₆ alkyl) and (C₁-C₄ alkyl) moieties in the foregoing R⁴ groups may optionally contain one or two double or triple bonds and may optionally be substituted with one or two substituents independently selected from hydroxy, amino, C₁-C₃ alkoxy, dimethylamino, methylamino, ethylamino, 20 -NHC(=O)CH₃, fluoro, chloro, C₁-C₃ thioalkyl, -CN, -COOH, -C(=O)O(C₁-C₄ alkyl), -C(=O)(C₁-C₄ alkyl) and -NO₂;

- R⁵ is phenyl, naphthyl, thienyl, benzothienyl, pyridyl, quinolyl, pyrazinyl, furanyl, benzofuranyl, benzothiazolyl, benzisothiazolyl, benzisoxazolyl, benzimidazolyl, indolyl, benzoxazolyl or C₃-C₈ cycloalkyl wherein one or two of the 25 carbon atoms of said cycloalkyl rings that contain at least 5 ring members may optionally and independently be replaced by an oxygen or sulfur atom or by NZ⁴ wherein Z⁴ is hydrogen, C₁-C₄ alkyl or benzyl; and wherein each of the foregoing R⁵ groups is substituted with from one to four substituents R¹² wherein one to three of said substituents may be selected, independently, from chloro, C₁-C₆ alkyl and -O(C₁-C₆ alkyl) and one of said substituents may be selected from bromo, iodo, formyl, -CN, 30 -CF₃, -NO₂, -NH₂, -NH(C₁-C₄ alkyl), -N(C₁-C₂ alkyl)(C₁-C₆ alkyl), -C(=O)O(C₁-C₄ alkyl), -C(=O)(C₁-C₄ alkyl), -COOH, -SO₂NH(C₁-C₄ alkyl), -SO₂N(C₁-C₂ alkyl)(C₁-C₄ alkyl), -SO₂NH₂, -NHSO₂(C₁-C₄ alkyl), -S(C₁-C₆ alkyl) and -SO₂(C₁-C₆ alkyl), and wherein each of the C₁-C₄ alkyl and C₁-C₆ alkyl moieties in the foregoing R⁵ groups may

optionally be substituted with one or two substituents independently selected from fluoro, hydroxy, amino, methylamino, dimethylamino and acetyl;

R^7 is hydrogen, C_1 - C_4 alkyl, halo, cyano, hydroxy, $-O(C_1$ - C_4 alkyl) $-C(=O)(C_1$ - C_4 alkyl), $-C(=O)O(C_1$ - C_4 alkyl), $-OCF_3$, $-CF_3$, $-CH_2OH$, $-CH_2O(C_1$ - C_4 alkyl);

5 R^{10} is hydrogen, hydroxy, methoxy or fluoro;

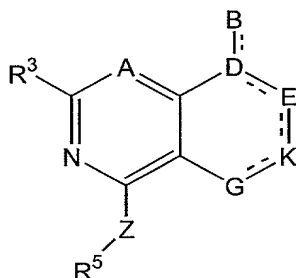
R^{11} is hydrogen or C_1 - C_4 alkyl; and

Z is NH, oxygen, sulfur, $-N(C_1$ - C_4 alkyl), $-NC(=O)(C_1$ - C_2 alkyl), $NC(=O)O(C_1$ - C_2 alkyl) or $CR^{13}R^{14}$ wherein R^{13} and R^{14} are independently selected from hydrogen, trifluoromethyl and methyl with the exception that one of R^{13} and R^{14} can be cyano;

10 with the proviso that: (a) in the five membered rings of structures I, II and III, there can not be two double bonds adjacent to each other; and (b) when R^4 is attached to nitrogen, it is not halo, cyano or nitro;

or a pharmaceutically acceptable salt of such compound.

15 7. A pharmaceutical composition according to claim 1 wherein said corticotropin releasing factor antagonist is a compound of formula



wherein the dashed lines represent optional double bonds;

A is nitrogen or CR^7 ;

20 B is $-NR^1R^2$, $-CR^1R^2R^{10}$, $-C(=CR^2R^{11})R^1$, $-NHCR^1R^2R^{10}$, $-OCR^1R^2R^{10}$, $-SCR^1R^2R^{10}$, $-CR^2R^{10}NHR^1$, $-CR^2R^{10}OR^1$, $-CR^2R^{10}SR^1$ or $-COR^2$, and is single bonded to D; or B is $-CR^1R^2$, and is double bonded to D and D is carbon;

D is nitrogen or CR^4 and is single bonded to all atoms to which it is attached, or D is carbon and is double bonded to E or double bonded to B;

25 E is oxygen, nitrogen, sulfur, $C=O$, $C=S$, CR^6R^{12} , NR^6 or CR^6 ; or E is a two atom spacer, wherein one of the atoms is oxygen, nitrogen, sulfur, $C=O$, $C=S$, CR^6R^{12} , NR^6 or CR^6 , and the other is CR^6R^{12} or CR^9 ;

K and G are each, independently, C=O, C=S, sulfur, oxygen, CHR⁸ or NR⁸ when single bonded to both adjacent ring atoms, or nitrogen or CR⁸ when it is double bonded to an adjacent ring atom;

the 6- or 7-membered ring that contains D, E, K and G may contain from one
5 to three double bonds, from zero to two heteroatoms selected from oxygen, nitrogen and sulfur, and from zero to two C=O or C=S groups, wherein the carbon atoms of such groups are part of the ring and the oxygen and sulfur atoms are substituents on the ring;

R¹ is C₁-C₆ alkyl optionally substituted with from one or two substituents
10 independently selected from hydroxy, fluoro, chloro, bromo, iodo, C₁-C₄ alkoxy, CF₃, -C(=O)(C₁-C₄alkyl), -C(=O)-O-(C₁-C₄)alkyl, -OC(=O)(C₁-C₄ alkyl), -OC(=O)N(C₁-C₄ alkyl)(C₁-C₂ alkyl), -NHCO(C₁-C₄ alkyl), -COOH, -COO(C₁-C₄ alkyl), -CONH(C₁-C₄ alkyl), -CON(C₁-C₄ alkyl)(C₁-C₂ alkyl), -S(C₁-C₄ alkyl), -CN, -NO₂, -SO(C₁-C₄ alkyl), -SO₂(C₁-C₄ alkyl), -SO₂NH(C₁-C₄ alkyl) and -SO₂N(C₁-C₄ alkyl)(C₁-C₂ alkyl), wherein
15 each of the C₁-C₄ alkyl groups in the foregoing R¹ groups may optionally contain one or two double or triple bonds;

R² is C₁-C₁₂ alkyl which may optionally contain from one to three double or triple bonds, aryl or (C₁-C₄ alkylene)aryl, wherein said aryl and the aryl moiety of said (C₁-C₄ alkylene)aryl is selected from phenyl, naphthyl, thienyl, benzothienyl, pyridyl,
20 quinolyl, pyrazinyl, pyrimidinyl, imidazolyl, furanyl, benzofuranyl, benzothiazolyl, isothiazolyl, pyrazolyl, pyrrolyl, indolyl, pyrrolopyridyl, oxazolyl and benzoxazolyl; C₃-C₈ cycloalkyl or (C₁-C₆ alkylene)(C₃-C₈ cycloalkyl), wherein one or two of the carbon atoms of said cycloalkyl and the 5 to 8 membered cycloalkyl moieties of said (C₁-C₆ alkylene)(C₃-C₈ cycloalkyl) may optionally and independently be replaced by an
25 oxygen or sulfur and wherein each of the foregoing R² groups may optionally be substituted with from one to three substituents independently selected from chloro, fluoro, hydroxy and C₁-C₄ alkyl, or with one substituent selected from C₁-C₆ alkoxy, -OC(=O)(C₁-C₆ alkyl), -OC(=O)N(C₁-C₄ alkyl)(C₁-C₂ alkyl), -S(C₁-C₆ alkyl), amino, -NH(C₁-C₂ alkyl), -N(C₁-C₂ alkyl)(C₁-C₄ alkyl), -N(C₁-C₄ alkyl)-CO-(C₁-C₄ alkyl),
30 -NHCO(C₁-C₄ alkyl), -COOH, -COO(C₁-C₄ alkyl), -CONH(C₁-C₄ alkyl), -CON(C₁-C₄ alkyl)(C₁-C₂ alkyl), -SH, -CN, -NO₂, -SO(C₁-C₄ alkyl), -SO₂(C₁-C₄ alkyl), -SO₂NH(C₁-C₄ alkyl) and -SO₂N(C₁-C₄ alkyl)(C₁-C₂ alkyl);

-NR¹R² or CR¹R²R¹⁰ may form a ring selected from saturated 3 to 8 membered rings, the 5 to 8 membered rings of which may optionally contain one or

two double bonds, and wherein one or two of the ring carbon atoms of such 5 to 8 membered rings may optionally and independently be replaced by an oxygen or sulfur atom or by NZ^3 wherein Z^3 is hydrogen or C_1-C_4 alkyl;

R^3 is hydrogen, C_1-C_4 alkyl, $-O(C_1-C_4 \text{ alkyl})$, chloro, fluoro, bromo, iodo,
5 $-S(C_1-C_4 \text{ alkyl})$ or $-SO_2(C_1-C_4 \text{ alkyl})$;
 R^4 is hydrogen, C_1-C_2 alkyl, hydroxy or fluoro;
each R^6 , R^8 and R^9 that is attached to a carbon atom is selected,
independently, from hydrogen, C_1-C_2 alkyl, fluoro, chloro, bromo, iodo, hydroxy,
hydroxymethyl, formyl, trifluoromethyl, cyano, amino, nitro, $-O(C_1-C_2 \text{ alkyl})$, $-N(C_1-C_2$
10 $\text{alkyl})(C_1-C_2 \text{ alkyl})$, $-S(C_1-C_2 \text{ alkyl})$, $-CO(C_1-C_2 \text{ alkyl})$, $-C(=O)H$ or $-C(=O)O(C_1-C_2 \text{ alkyl})$,
wherein each of the C_1-C_2 alkyl moieties in the foregoing R^6 , R^8 , and R^9 groups may
optionally contain one double or triple bond; and each R^6 , R^8 , and R^9 that is attached
to a nitrogen atom is selected, independently, from hydrogen and C_1-C_4 alkyl;

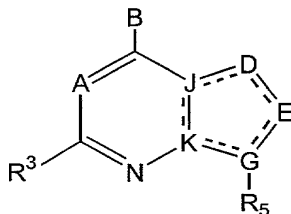
R^5 is substituted phenyl, naphthyl, pyridyl or pyrimidyl, wherein each of the
15 foregoing R^5 groups is substituted with from two to four substituents R^{15} , wherein
from one to three of said substituents may be selected, independently, from chloro,
 C_1-C_6 alkyl, $-O(C_1-C_6 \text{ alkyl})$ and $-(C_1-C_6\text{alkylene})O(C_1-C_6\text{alkyl})$, and wherein one of
said substituents may be selected, independently, from bromo, iodo, formyl, cyano,
trifluoromethyl, nitro, amino, $-NH(C_1-C_4 \text{ alkyl})$, $-N(C_1-C_2 \text{ alkyl})(C_1-C_6 \text{ alkyl})$,
20 $-C(=O)O(C_1-C_4 \text{ alkyl})$, $-C(=O)(C_1-C_4 \text{ alkyl})$, $-COOH$, $-SO_2NH(C_1-C_4 \text{ alkyl})$,
 $-SO_2N(C_1-C_2 \text{ alkyl})(C_1-C_4 \text{ alkyl})$, $-SO_2NH_2$, $-NHSO_2(C_1-C_4 \text{ alkyl})$, $-S(C_1-C_6 \text{ alkyl})$ and
 $-SO_2(C_1-C_6 \text{ alkyl})$, and wherein each of the C_1-C_4 alkyl and C_1-C_6 alkyl moieties in the
foregoing R^5 groups may optionally be substituted with one or two substituents
independently selected from fluoro, hydroxy, amino, methylamino, dimethylamino and
25 acetyl;

R^7 is hydrogen, methyl, halo, hydroxy, methoxy, $-C(=O)(C_1-C_2 \text{ alkyl})$,
 $-C(=O)O(C_1-C_2 \text{ alkyl})$, trifluoromethoxy, hydroxymethyl, trifluoromethyl or formyl;
 R^{10} is hydrogen, hydroxy, methoxy or fluoro;
 R^{11} is hydrogen or C_1-C_4 alkyl;
30 R^{12} is hydrogen or methyl; and
 Z is NH , oxygen, sulfur, $-N(C_1-C_4 \text{ alkyl})$, or $CR^{13}R^{14}$ wherein R^{13} and R^{14} are
independently selected from hydrogen, and methyl with the exception that one of R^{13}
and R^{14} may optionally be cyano;

with the proviso that: (a) in the six or seven membered rings of structures in formula I, there can not be two double bonds adjacent to each other; and (b) when D is carbon and is double bonded to B, then B is CR^1R^2 ;
or a pharmaceutically acceptable salt of such compound.

5

8. A pharmaceutical composition according to claim 1 wherein said corticotropin releasing factor antagonist is a compound of formula



or a pharmaceutically acceptable salt thereof, wherein

10

the dashed lines represent optional double bonds;

A is nitrogen or CR^7 ;

B is $-\text{NR}^1\text{R}^2$, $-\text{CR}^1\text{R}^2\text{R}^{10}$, $-\text{C}(=\text{CR}^2\text{R}^{11})\text{R}^1$, $-\text{NHCR}^1\text{R}^2\text{R}^{10}$, $-\text{OCR}^1\text{R}^2\text{R}^{10}$, $-\text{SCR}^1\text{R}^2\text{R}^{10}$, $-\text{CR}^2\text{R}^{10}\text{NHR}^1$, $-\text{CR}^2\text{R}^{10}\text{OR}^1$, $-\text{CR}^2\text{R}^{10}\text{SR}^1$ or $-\text{COR}^2$;

15

J and K are each independently nitrogen or carbon and both J and K are not nitrogens;

D and E are each selected, independently, from nitrogen, CR^4 , $\text{C}=\text{O}$, $\text{C}=\text{S}$, sulfur, oxygen, CR^4R^6 and NR^8 ;

G is nitrogen or carbon;

20

the ring containing D, E, G, K, and J in formula I may be a saturated or unsaturated 5-membered ring and may optionally contain one or two double bonds and may optionally contain from one to three heteroatoms in the ring and may optionally have one or two $\text{C}=\text{O}$ or $\text{C}=\text{S}$ groups;

25

R^1 is $\text{C}_1\text{-C}_6$ alkyl optionally substituted with one or two substituents independently selected from hydroxy, fluoro, chloro, bromo, iodo, $-\text{O}(\text{C}_1\text{-C}_4 \text{ alkyl})$, CF_3 , $-\text{C}(=\text{O})\text{O}(\text{C}_1\text{-C}_4 \text{ alkyl})$, $-\text{OC}(=\text{O})(\text{C}_1\text{-C}_4 \text{ alkyl})$, $-\text{OC}(=\text{O})\text{N}(\text{C}_1\text{-C}_4 \text{ alkyl})(\text{C}_1\text{-C}_2 \text{ alkyl})$, $-\text{NHCO}(\text{C}_1\text{-C}_4 \text{ alkyl})$, $-\text{COOH}$, $-\text{COO}(\text{C}_1\text{-C}_4 \text{ alkyl})$, $-\text{CONH}(\text{C}_1\text{-C}_4 \text{ alkyl})$, $-\text{CON}(\text{C}_1\text{-C}_4 \text{ alkyl})(\text{C}_1\text{-C}_2 \text{ alkyl})$, $-\text{S}(\text{C}_1\text{-C}_4 \text{ alkyl})$, $-\text{CN}$, $-\text{NO}_2$, $-\text{SO}(\text{C}_1\text{-C}_4 \text{ alkyl})$, $-\text{SO}_2(\text{C}_1\text{-C}_4 \text{ alkyl})$, $-\text{SO}_2\text{NH}(\text{C}_1\text{-C}_4 \text{ alkyl})$ and $-\text{SO}_2\text{N}(\text{C}_1\text{-C}_4 \text{ alkyl})(\text{C}_1\text{-C}_2 \text{ alkyl})$, wherein each of the $\text{C}_1\text{-C}_4$ alkyl groups in the foregoing R^1 groups may optionally contain one or two double or triple bonds;

30

- R^2 is C_1 - C_{12} alkyl which may optionally contain from one to three double or triple bonds, aryl or $(C_1$ - C_4 alkylene)aryl, wherein said aryl and the aryl moiety of said $(C_1$ - C_4 alkylene)aryl is selected from phenyl, naphthyl, thienyl, benzothienyl, pyridyl, quinolyl, pyrazinyl, pyrimidinyl, imidazolyl, furanyl, benzofuranyl, benzothiazolyl, isothiazolyl, pyrazolyl, pyrrolyl, indolyl, pyrrolopyridyl, oxazolyl and benzoxazolyl;
- 5 C_3 - C_8 cycloalkyl or $(C_1$ - C_6 alkylene)(C_3 - C_8 cycloalkyl), wherein one or two of the carbon atoms of said cycloalkyl and the 5 to 8 membered cycloalkyl moieties of said $(C_1$ - C_6 alkylene)(C_3 - C_8 cycloalkyl) may optionally and independently be replaced by an oxygen or sulfur atom or by NZ^2 wherein Z^2 is selected from hydrogen, C_1 - C_4 alkyl, benzyl and C_1 - C_4 alkanoyl, and wherein each of the foregoing R^2 groups may optionally be substituted with from one to three substituents independently selected from chloro, fluoro, hydroxy and C_1 - C_4 alkyl, or with one substituent selected from bromo, iodo, C_1 - C_6 alkoxy, $-OC(=O)(C_1$ - C_6 alkyl), $-OC(=O)N(C_1$ - C_4 alkyl)(C_1 - C_2 alkyl), $-S(C_1$ - C_6 alkyl), amino, $-NH(C_1$ - C_2 alkyl), $-N(C_1$ - C_2 alkyl)(C_1 - C_4 alkyl), $-N(C_1$ - C_4 alkyl)-CO-(C_1 - C_4 alkyl), $-NHCO(C_1$ - C_4 alkyl), $-COOH$, $-COO(C_1$ - C_4 alkyl), $-CONH(C_1$ - C_4 alkyl), $-CON(C_1$ - C_4 alkyl)(C_1 - C_2 alkyl), $-SH$, $-CN$, $-NO_2$, $-SO(C_1$ - C_4 alkyl), $-SO_2(C_1$ - C_4 alkyl), $-SO_2NH(C_1$ - C_4 alkyl) and $-SO_2N(C_1$ - C_4 alkyl)(C_1 - C_2 alkyl);
- 15 $-NR^1R^2$ or $CR^1R^2R^{10}$ may form a saturated 3 to 8 membered carbocyclic ring which may optionally contain from one to three double bonds and wherein one or two of the ring carbon atoms of such 5 to 8 membered rings may optionally and independently be replaced by an oxygen or sulfur atom or by NZ^3 wherein Z^3 is hydrogen, C_1 - C_4 alkyl, benzyl or C_1 - C_4 alkanoyl;
- 20 R^3 is hydrogen, C_1 - C_4 alkyl, $-O(C_1$ - C_4 alkyl), chloro, fluoro, bromo, iodo, $(C_1$ - C_2 alkylene)-O-(C_1 - C_2 alkyl), $(C_1$ - C_2 alkylene)-OH, or $-S(C_1$ - C_4 alkyl);
- 25 each R^4 is, independently, hydrogen, $(C_1$ - C_6 alkyl), fluoro, chloro, bromo, iodo, hydroxy, cyano, amino, $(C_1$ - C_2 alkylene)-OH, CF_3 , CH_2SCH_3 , nitro, $-O(C_1$ - C_4 alkyl), $-N(C_1$ - C_4 alkyl)(C_1 - C_2 alkyl), $-S(C_1$ - C_4 alkyl), $-CO(C_1$ - C_4 alkyl), $-C(=O)H$ or $-C(=O)O(C_1$ - C_4 alkyl);
- R^6 is hydrogen, methyl or ethyl;
- 30 R^8 is hydrogen or C_1 - C_4 alkyl;
- R^5 is phenyl, pyridyl, pyrazinyl, pyrimidyl, pyridazinyl and wherein each of the foregoing R^5 groups is substituted with from one to four substituents R^{13} wherein one to three of said substituents may be selected, independently, from fluoro, chloro, C_1 - C_6 alkyl and $-O(C_1$ - C_6 alkyl) and one of said substituents may be selected from

bromo, iodo, formyl, OH, (C₁-C₄ alkylene)-OH, (C₁-C₄alkylene)-O-(C₁-C₂ alkyl), -CN, -CF₃, -NO₂, -NH₂, -NH(C₁-C₄ alkyl), -N(C₁-C₂ alkyl)(C₁-C₆ alkyl), -OCO(C₁-C₄ alkyl), (C₁-C₄ alkylene)-O-(C₁-C₄ alkyl), -S(C₁-C₆ alkyl), (C₁-C₄ alkylene)-S-(C₁-C₄ alkyl), -C(=O)O(C₁-C₄ alkyl), -C(=O)(C₁-C₄ alkyl), -COOH, -SO₂NH(C₁-C₄ alkyl),

- 5 -SO₂N(C₁-C₂ alkyl)(C₁-C₄ alkyl), -SO₂NH₂, -NHSO₂(C₁-C₄ alkyl), -S(C₁-C₆ alkyl) and -SO₂(C₁-C₆ alkyl), and wherein each of the C₁-C₄ alkyl and C₁-C₆ alkyl moieties in the foregoing R⁵ groups may optionally have one or two double bonds;

R⁷ is hydrogen, C₁-C₄ alkyl, halo (e.g., chloro, fluoro, iodo or bromo), hydroxy, -O(C₁-C₄ alkyl), -C(=O)(C₁-C₄ alkyl), -C(=O)O(C₁-C₄ alkyl), -OCF₃, -CF₃, -CH₂OH or

- 10 -CH₂O(C₁-C₂ alkyl);

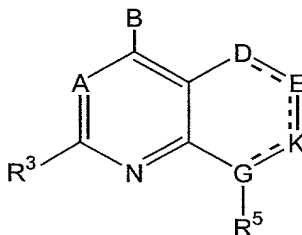
R¹⁰ is hydrogen, hydroxy, methoxy or fluoro;

R¹¹ is hydrogen or C₁-C₄ alkyl; and

with the proviso that: a) when both J and K are carbons and D is CR⁴ and E is nitrogen, then G can not be nitrogen; (b) when both J and K are carbons and D and G are nitrogens, then E can not be CR⁴ or C=O or C=S; (c) when both J and K are carbons and D and E are carbons, then G can not be nitrogen; (d) when G is carbon, it must be double banded to E; and (e) in the ring containing J, K, D, E and G, there can not be two double bonds adjacent to each other;

- 20 and the pharmaceutically acceptable salts of such compounds.

9. A pharmaceutical composition according to claim 1 wherein said corticotropin releasing factor antagonist is a compound of formula



wherein the dashed lines represent optional double bonds;

- 25 A is nitrogen or CR⁷;

B is -NR¹R², -CR¹R²R¹⁰, -C(=CR²R¹¹)R¹, -NHC(R¹R²R¹⁰), -OCR¹R²R¹⁰, -SCR¹R²R¹⁰, -CR²R¹⁰NHR¹, -CR²R¹⁰OR¹, -CR²R¹⁰SR¹ or -COR²;

G is nitrogen or CR⁴ and is single bonded to all atoms to which it is attached, or G is carbon and is double bonded to K;

K is nitrogen or CR⁶ when double bonded to G or E, or K is oxygen, sulfur, C=O, C=S, CR⁶R¹² or NR⁸ when single bonded to both adjacent ring atoms, or K is a two atom spacer, wherein one of the two ring atoms of the spacer is oxygen, nitrogen, sulfur, C=O, C=S, CR⁶R¹², NR⁶ or CR⁶, and the other is CR⁶R¹² or CR⁸;

- 5 D and E are each, independently, C=O, C=S, sulfur, oxygen, CR⁴R⁶ or NR⁸ when single bonded to both adjacent ring atoms, or nitrogen or CR⁴ when it is double bonded to an adjacent ring atom;

- the 6- or 7-membered ring that contains D, E, K and G may contain from one to three double bonds, from zero to two heteroatoms selected from oxygen, nitrogen and sulfur, and from zero to two C=O or C=S groups, wherein the carbon atoms of such groups are part of the ring and the oxygen and sulfur atoms are substituents on the ring;

- R¹ is C₁-C₆ alkyl optionally substituted with from one or two substituents independently selected from hydroxy, fluoro, chloro, bromo, iodo, C₁-C₄ alkoxy, CF₃,
15 -C(=O)(C₁-C₄alkyl), -C(=O)-O-(C₁-C₄)alkyl, -OC(=O)(C₁-C₄ alkyl), -OC(=O)N(C₁-C₄ alkyl)(C₁-C₂ alkyl), -NHCO(C₁-C₄ alkyl), -COOH, -COO(C₁-C₄ alkyl), -CONH(C₁-C₄ alkyl), -CON(C₁-C₄ alkyl)(C₁-C₂ alkyl), -S(C₁-C₄ alkyl), -CN, -NO₂, -SO(C₁-C₄ alkyl), -SO₂(C₁-C₄ alkyl), -SO₂NH(C₁-C₄ alkyl) and -SO₂N(C₁-C₄ alkyl)(C₁-C₂ alkyl), wherein each of the C₁-C₄ alkyl groups in the foregoing R¹ groups may optionally contain one
20 or two double or triple bonds;

- R² is C₁-C₁₂ alkyl which may optionally contain from one to three double or triple bonds, aryl or (C₁-C₄ alkylene)aryl, wherein said aryl and the aryl moiety of said (C₁-C₄ alkylene)aryl is selected from phenyl, naphthyl, thienyl, benzothienyl, pyridyl, quinolyl, pyrazinyl, pyrimidinyl, imidazolyl, furanyl, benzofuranyl, benzothiazolyl, isothiazolyl, pyrazolyl, pyrrolyl, indolyl, pyrrolopyridyl, oxazolyl and benzoxazolyl;
25 C₃-C₈ cycloalkyl or (C₁-C₆ alkylene)(C₃-C₈ cycloalkyl), wherein one or two of the carbon atoms of said cycloalkyl and the 5 to 8 membered cycloalkyl moieties of said (C₁-C₆ alkylene)(C₃-C₈ cycloalkyl may optionally and independently be replaced by an oxygen or sulfur atom or by NZ wherein Z is hydrogen, C₁-C₄ alkyl or benzyl, and
30 wherein each of the foregoing R² groups may optionally be substituted with from one to three substituents independently selected from chloro, fluoro, hydroxy and C₁-C₄ alkyl, or with one substituent selected from C₁-C₆ alkoxy, -OC(=O)(C₁-C₆ alkyl), -OC(=O)N(C₁-C₄ alkyl)(C₁-C₂ alkyl), -S(C₁-C₆ alkyl), amino, -NH(C₁-C₂ alkyl), -N(C₁-C₂ alkyl)(C₁-C₄ alkyl), -N(C₁-C₄ alkyl)-CO-(C₁-C₄ alkyl), -NHCO(C₁-C₄ alkyl), -COOH,

-COO(C₁-C₄ alkyl), -CONH(C₁-C₄ alkyl), -CON(C₁-C₄ alkyl)(C₁-C₂ alkyl), -SH, -CN, -NO₂, -SO(C₁-C₄ alkyl), -SO₂(C₁-C₄ alkyl), -SO₂NH(C₁-C₄ alkyl) and -SO₂N(C₁-C₄ alkyl)(C₁-C₂ alkyl);

-NR¹R² or CR¹R²R¹⁰ may form a ring selected from saturated 3 to 8

- 5 membered rings, the 5 to 8 membered rings of which may optionally contain one or two double bonds, and wherein one or two of the ring carbon atoms of such 5 to 8 membered rings may optionally and independently be replaced by an oxygen or sulfur atom or by NZ² wherein Z² is hydrogen, benzyl or C₁-C₄ alkyl;

R³ is hydrogen, C₁-C₄ alkyl, -O(C₁-C₄ alkyl), chloro, fluoro, bromo, iodo,

- 10 -S(C₁-C₄ alkyl) or -SO₂(C₁-C₄ alkyl);

each R⁸, R⁹ and R¹² is selected, independently, from hydrogen and C₁-C₂ alkyl;

each R⁴ and R⁶ that is attached to a carbon atom is selected, independently, from hydrogen and C₁-C₆ alkyl, fluoro, chloro, bromo, iodo, hydroxy, hydroxy (C₁-C₂ alkyl), trifluoromethyl, cyano, amino, nitro, -O(C₁-C₄ alkyl), -N(C₁-C₄ alkyl)(C₁-C₂ alkyl), -CH₂SCH₃, -S(C₁-C₄ alkyl), -CO(C₁-C₄ alkyl), -C(=O)H or -C(=O)O(C₁-C₄ alkyl), wherein each of the C₁-C₂ alkyl moieties in the foregoing R⁴ and R⁶ groups may optionally contain one double or triple bond; and R⁶, when attached to a nitrogen atom, is selected from hydrogen and C₁-C₄ alkyl;

- 20 R⁵ is substituted phenyl, naphthyl, pyridyl or pyrimidyl, wherein each of the foregoing R⁵ groups is substituted with from two to four substituents R¹³, wherein up to three of said substituents may be selected, independently, from chloro, C₁-C₆ alkyl, -O(C₁-C₆ alkyl) and -(C₁-C₆ alkylene)O(C₁-C₆alkyl), and wherein one of said substituents may be selected, independently, from bromo, iodo, formyl, cyano,
- 25 trifluoromethyl, nitro, amino, -NH(C₁-C₄ alkyl), -N(C₁-C₂ alkyl)(C₁-C₆ alkyl), -C(=O)O(C₁-C₄ alkyl), -C(=O)(C₁-C₄ alkyl), -COOH, -SO₂NH(C₁-C₄ alkyl), -SO₂N(C₁-C₂ alkyl)(C₁-C₄ alkyl), -SO₂NH₂, -NH₂SO₂(C₁-C₄ alkyl), -(C₀-C₁alkylene)-S-(C₁-C₂alkyl), -(C₀-C₁alkylene)-SO-(C₁-C₂alkyl), -(C₀-C₁alkylene)-SO₂-(C₁-C₂alkyl) and -(C₁-C₄alkylene)-OH, and wherein each of the C₁-C₄ alkyl and C₁-C₆ alkyl moieties in
- 30 the foregoing R⁵ groups may optionally be substituted with one or two substituents independently selected from fluoro, hydroxy, amino, methylamino, dimethylamino and acetyl;

R^7 is hydrogen, methyl, halo (e.g., chloro, fluoro, iodo or bromo), hydroxy, methoxy, $-C(=O)(C_1-C_2 \text{ alkyl})$, $-C(=O)O(C_1-C_2 \text{ alkyl})$, hydroxymethyl, trifluoromethyl or formyl;

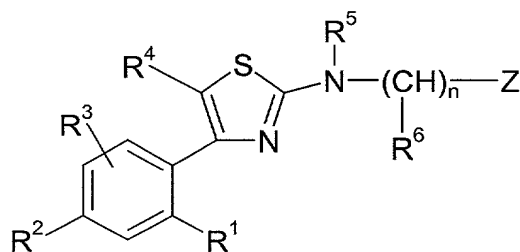
R^{10} is hydrogen, hydroxy, methoxy or fluoro; and

5 R^{11} is hydrogen or C_1-C_4 alkyl;

with the proviso that in the ring containing D, E, K and G of formula I, there can not be two double bonds adjacent to each other;

and the pharmaceutically acceptable salt of such compound.

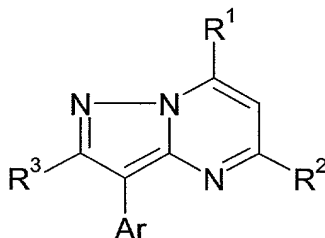
10 10. A pharmaceutical composition according to claim 1 wherein said corticotropin releasing factor antagonist is a compound of formula



wherein each of R^1 and R^2 is independently a halogen atom; a C_1-C_5 hydroxyalkyl radical; C_1-C_5 alkyl; C_7-C_{10} aralkyl; C_1-C_5 alkoxy; trifluoromethyl; nitro; nitrile; a group -SR where R is hydrogen, a C_1-C_5 alkyl radical or a C_7-C_{10} aralkyl radical; a group S-CO-R where R is a C_1-C_5 alkyl radical or aralkyl in which the aryl portion is C_6-C_8 and the alkyl portion is C_1-C_4 ; a group $-COOR'$ where R' is hydrogen or C_1-C_5 alkyl; a group $-CONR'R''$ where R' and R'' are as defined above for R' ; a group $-NR'R''$ where R' and R'' are as previously defined for R' ; a group $-CONRaRb$ or $NRaRb$, where Ra and Rb, taken together with the nitrogen atom to which they are attached, form a 5- to 7-membered heterocyclic ring; or a group $-NHCO-NR'R''$, where R' and R'' are as defined above for R' ; R^3 is hydrogen or as defined for R^1 and R^2 is a hydrogen atom; C_{1-5} alkyl; halogen; a hydroxymethyl group; or a formyl group; R^5 is C_1-C_5 alkyl; a C_3-C_7 cycloalkyl group; a cycloalkylalkyl group in which the cycloalkyl portion is C_3-C_7 and the alkyl portion is C_1-C_5 ; or C_5-C_6 alkenyl; n is 0 or 1; R^6 is C_{1-5} alkyl; alkoxyalkyl in which the alkyl portions are C_1-C_5 ; C_3-C_7 cycloalkyl; a cycloalkylalkyl group in which the cycloalkyl portion is C_3-C_7 and the alkyl portion is C_1-C_5 ; a cycloalkyloxyalkyl radical in which the cycloalkyl is C_3-C_7 and the alkyl is C_1-C_4 ; a hydroxyalkyloxyalkyl radical in which the alkyls are C_2-C_{10} ; or an alkoxyalkyloxyalkyl radical in which the

alkyls are C₃-C₁₂; and Z is an optionally substituted bi- or tricyclic aromatic or heteroaromatic group; and stereoisomers and/or addition salts thereof.

11. A pharmaceutical composition according to claim 1 wherein said
5 corticotropin releasing factor antagonist is a compound of formula



including the stereoisomers and the pharmaceutically acceptable acid addition salt forms thereof, wherein

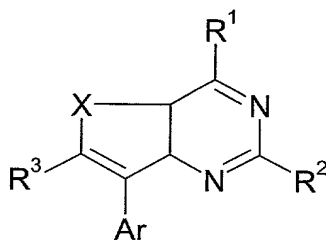
- R¹ is NR⁴R⁵ or OR⁵;
10 R² is C₁-C₆alkyl, C₁-C₆alkyloxy or C₁-C₆alkylthio,
R³ is hydrogen, C₁-C₆alkyl, C₁-C₆alkylsulfonyl, C₁-C₆alkylsulfoxy or C₁-C₆alkylthio;
R⁴ is hydrogen, C₁-C₆alkyl, mono- or di(C₃-C₆cycloalkylmethyl, C₃-C₆cyloalkyl, C₃-C₆alkenyl, hydroxyC₁-C₆alkyl, C₁-C₆alkylcarbonyloxyC₁-C₆alkyl or C₁-C₆alkyloxyC₁-C₆alkyl;
15 R⁵ is C₁-C₈alkyl, mono- or di(C₃-C₆cycloalkyl)methyl, Ar¹CH₂, C₃-C₆alkenyl, C₁-C₆alkyloxyC₁-C₆alkyl, hydroxyC₁-C₆alkyl, thienylmethyl, furanylmethyl, C₁-C₆alkylthioC₁-C₆alkyl, morpholinyl, mono- or di(C₁-C₆alkyl)aminoC₁₋₆alkyl, di(C₁-C₆alkyl)amino, C₁-C₆alkylcarbonylC₁-C₆alkyl, C₁-C₆alkyl substituted with imidazolyl; or
20 a radical of formula -Alk-O-CO-Ar¹;
or R⁴ and R⁵ taken together with the nitrogen atom to which they are attached may form a pyrrolidinyl, piperidinyl, homopiperidinyl or morpholinyl group, optionally substituted with C₁-C₆alkyl or C₁-C₆alkyloxyC₁-C₆alkyl; and
Ar is phenyl; phenyl substituted with 1, 2 or 3 substituents independently
25 selected from halo, C₁-C₆alkyl, trifluoromethyl, hydroxy, cyano, C₁-C₆alkyloxy, benzyloxy, C₁-C₆alkylthio, nitro, amino and mono- or di(C₁-C₆alkyl)amino; pyridinyl; pyridinyl substituted with 1 ~ 2 or 3 substituents independently selected from halo, C₁-C₆alkyl, trifluoromethyl, hydroxy, cyano, C₁-C₆alkyloxy, benzyloxy, C₁-C₆alkylthio,

nitro, amino, mono- or di(C₁-C₆alkyl)amino and piperidinyl; and wherein said substituted phenyl may optionally be further substituted with one or more halogens;

Ar¹ is phenyl; phenyl substituted with 1, 2 or 3 substituents each independently selected from halo, C₁-C₆alkyl, C₁-C₆alkyloxy, di(C₁-C₆alkyl)aminoC₁-C₆alkyl, trifluoromethyl and C₁-C₆alkyl substituted with morpholinyl; or pyridinyl; and Alk is C₁-C₆alkanediyl;

with the proviso that 5-methyl-3-phenyl-7-(phenylmethoxy)-pyrazolo[1,5-a]pyrimidine and 2,5-dimethyl-7-(methylamino)-3-phenyl-pyrazolo[1,5-a]pyrimidine are not included.

12. A pharmaceutical composition according to claim 1 wherein said corticotropin releasing factor antagonist is a compound of formula



including the stereoisomers and the pharmaceutically acceptable acid addition salt forms thereof, wherein

X is S, SO or SO₂;

R¹ is NR⁴R⁵ or OR⁵;

R² is C₁-C₆alkyl, C₁-C₆alkyloxy or C₁-C₆alkylthio;

R³ is hydrogen, C₁-C₆alkyl, C₁-C₆alkylsulfonyl, C₁-C₆alkylsulfoxy or C₁-C₆alkylthio;

R⁴ is hydrogen, C₁₋₆alkyl, mono- or di(C₃-C₆cycloalkyl)methyl, C₃-C₆cycloalkyl, C₃-C₆alkenyl, hydroxyC₁-C₆alkyl, C₁-C₆alkylcarbonyloxyC₁-C₆alkyl or C₁-C₆alkyloxyC₁-C₆alkyl;

R⁵ is C₁-C₈alkyl, mono- or di(C₃-C₆cycloalkyl)methyl, Ar¹CH₂, C₃-C₆alkenyl, C₁-C₆alkyloxyC₁-C₆alkyl, hydroxyC₁-C₆alkyl, thienylmethyl, furanylmethyl, C₁-C₆alkylthioC₁-C₆alkyl, morpholinyl, mono- or di(C₁-C₆alkyl)aminoC₁-C₆alkyl, di(C₁-C₆alkyl)amino, C₁-C₆alkylcarbonylC₁-C₆alkyl, C₁-C₆alkyl substituted with imidazolyl; or a radical of formula -Alk-O-CO-Ar I;

or R⁴ and R⁵ taken together with the nitrogen atom to which they are attached may form a pyrrolidinyl, piperidinyl, homopiperidinyl or morpholinyl group, optionally substituted with C₁-C₆alkyl or C₁-C₆alkyloxyC₁-C₆alkyl;

Ar is phenyl; phenyl substituted with 1, 2 or 3 substituents independently
 5 selected from halo, C₁-C₆alkyl, trifluoromethyl, hydroxy, cyano, C₁-C₆alkyloxy, benzyloxy, C₁-C₆alkylthio, nitro, amino and mono- or di(C₁-C₆alkyl)amino; pyridinyl; pyridinyl substituted with 1, 2 or 3 substituents independently selected from halo, C₁-C₆alkyl, trifluoromethyl, hydroxy, cyano, C₁-C₆alkyloxy, benzyloxy, C₁-C₆alkylthio, nitro, amino, mono- or di(C₁-C₆alkyl)amino and piperidinyl; and wherein said
 10 substituted phenyl may optionally be further substituted with one or more halogens;

Ar¹ is phenyl; phenyl substituted with 1, 2 or 3 substituents each independently selected from halo, C₁-C₆alkyl, C₁-C₆alkyloxy, di(C₁-C₆alkyl)aminoC₁-C₆alkyl trifluoromethyl, and C₁-C₆alkyl substituted with morpholinyl; or pyridinyl; and Alk is C₁-C₆alkanediyl.

15

13. A pharmaceutical composition according to claim 1 wherein said corticotropin releasing factor antagonist is a compound selected from the group consisting of:

- 20 4-(1-ethyl-propoxy)-3,6-dimethyl-2-(2,4,6-trimethylphenoxy)-pyridine;
 butyl-[2,5-dimethyl-7-(2,4,6-trimethylphenyl)-6,7-dihydro-5H-pyrrolo[2,3-d]pyrimidin-4-yl]-ethyl-amine;
 4-(butyl-ethylamino)-2,5-dimethyl-7-(2,4,6-trimethylphenyl)-5,7-dihydro-pyrrolo[2,3-d]pyrimidin-6-one;
 4-(1-ethylpropoxy)-2,5-dimethyl-6-(2,4,6-trimethylphenoxy)-pyrimidine;
 25 N-butyl-N-ethyl-2,5-dimethyl-NN-(2,4,6-trimethylphenyl)-pyrimidine-4,6-diamine;
 [4-(1-ethyl-propoxy)-3,6-dimethyl-pyridin-2-yl]-(2,4,6-trimethylphenyl)-amine;
 6-(ethyl-propyl-amino)-2,7-dimethyl-9-(2,4,6-trimethylphenyl)-7,9-dihydro-purin-8-one;
 30 3-[(4-methyl-benzyl)-[3,6-dimethyl-1-(2,4,6-trimethylphenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-yl]-amino}-propan-1-ol;
 diethyl-[6-methyl-3-methylsulfanyl-1-(2,4,6-trichlorophenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-yl]-amine;

- 2-{butyl-[6-methyl-3-methylsulfanyl-1-(2,4,6-trichlorophenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-yl]-amino}-ethanol;
- dibutyl-[6-methyl-3-methylsulfanyl-1-(2,4,6-trichlorophenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-yl]-amine;
- 5 butyl-ethyl-[6-methyl-3-methylsulfanyl-1-(2,4,6-trichlorophenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-yl]-amine;
- butyl-ethyl-[6-methyl-3-methylsulfonyl-1-(2,4,6-trichlorophenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-yl]-amine;
- butyl-cyclopropylmethyl-[6-methyl-3-methylsulfanyl-1-(2,4,6-trichlorophenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-yl]-amine;
- 10 di-1-propyl-[6-methyl-3-methylsulfanyl-1-(2,4,6-trichlorophenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-yl]-amine;
- diallyl-[6-methyl-3-methylsulfanyl-1-(2,4,6-trichlorophenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-yl]-amine;
- 15 butyl-ethyl-[6-chloro-3-methylsulfanyl-1-(2,4,6-trichlorophenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-yl]-amine;
- butyl-ethyl-[6-methoxy-3-methylsulfanyl-1-(2,4,6-trichlorophenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-yl]-amine;
- propyl-ethyl-[3,6-dimethyl-1-(2,4,6-trimethylphenyl)-1H-pyrazolo[3,4-d]pyrimidin-4-yl]-amine;
- 20 4-(1-ethyl-propyl)-6-methyl-3-methylsulfanyl-1-(2,4,6-trimethylphenyl)-1H-pyrazolo[3,4-d]pyrimidine;
- n-butyl-ethyl-[2,5-dimethyl-7-(2,4,6-trimethylphenyl)-7H-pyrrolo[2,3-d]pyrimidin-4-yl]amine;
- 25 di-n-propyl-[2,5-dimethyl-7-(2,4,6-trimethylphenyl)-7H-pyrrolo[2,3-d]pyrimidin-4-yl]amine;
- ethyl-n-propyl-[2,5-dimethyl-7-(2,4,6-trimethylphenyl)-7H-pyrrolo[2,3-d]pyrimidin-4-yl]amine;
- diethyl-2,5-dimethyl-7-(2,4,6-trimethylphenyl)-7H-pyrrolo[2,3-d]pyrimidin-4-yl]amine;
- 30 n-butyl-ethyl-[2,5,6-trimethyl-7-(2,4,6-trimethylphenyl)-7H-pyrrolo[2,3-d]pyrimidin-4-yl]amine;
- 2-{N-n-butyl-N-[2,5-dimethyl-7-(2,4,6-trimethylphenyl)-7H-pyrrolo[2,3-d]pyrimidin-4-yl]amino}-ethanol;

- 4-(1-ethyl-propyl)-2,5,6-trimethyl-7-(2,4,6-trimethylphenyl)-7H-pyrrolo[2,3-d]pyrimidine;
- n-butyl-ethyl-[2,5-dimethyl-7-(2,4-dimethylphenyl)-7H-pyrrolo[2,3-d]pyrimidin-4-yl]amine;
- 5 2,5-dimethyl-7-(2,4,6-trimethylphenyl)-7H-pyrrolo[2,3-d]pyrimidin-4-yl)-(1-ethyl-propyl)amine;
- butyl-[3,6-dimethyl-1-(2,4,6-trimethylphenyl)-1H-pyrazolo[3,4-b]pyridin-4-yl]-ethylamine;
- [3,6-dimethyl-1-(2,4,6-trimethylphenyl)-1H-pyrazolo[3,4-b]pyridin-4-yl]-(1-methoxymethylpropyl)-amine;
- 10 4-(1-methoxymethylpropoxy)-3,6-dimethyl-1-(2,4,6-trimethylphenyl)-1H-pyrazolo[3,4-b]pyridine;
- (1-ethylpropyl)-[3,5,6-trimethyl-1-(2,4,6-trimethylphenyl)-1H-pyrazolo[3,4-b]pyridin-4-yl]-amine;
- 15 4-(1-ethylpropoxy)-2,5-dimethyl-7-(2,4,6-trimethylphenyl)-7H-pyrrolo[2,3-b]pyridine;
- 4-(1-ethylpropoxy)-2,5,6-trimethyl-7-(2,4,6-trimethylphenyl)-7H-pyrrolo[2,3-b]pyridine;
- 4-(1-ethylpropoxy)-2,5-dimethyl-7-(2,6-dimethyl-4-bromophenyl)-7H-pyrrolo[2,3-b]pyridine;
- 20 2,5,6-trimethyl-7-(1-propylbutyl)-4-(2,4,6-trimethylphenoxy)-7H-pyrrolo[2,3-d]pyrimidine;
- 1-(1-ethylpropyl)-6-methyl-4-(2,4,6-trimethylphenylamino)-1,3-dihydro-imidazo[4,5-c]pyridin-2-one;
- 25 9-(1-ethylpropyl)-2-methyl-6-(2,4,6-trimethylphenylamino)-7,9-dihydro-purin-8-one;
- 1-(1-ethylpropyl)-6-methyl-4-(2,4,6-trimethylphenoxy)-1,3-dihydro-imidazo[4,5-c]pyridin-2-one;
- 1-(1-ethylpropyl)-6-methyl-4-(2,4,6-trimethylphenoxy)-1H-imidazo[4,5-c]pyridine;
- 30 1-(1-ethylpropyl)-3,6-dimethyl-4-(2,4,6-trimethylphenoxy)-1,3-dihydro-imidazo[4,5-c]pyridin-2-one;
- 1-(1-ethylpropyl)-3,6-dimethyl-4-(2,4,6-trimethylphenylamino)-1,3-dihydro-imidazo[4,5-c]pyridin-2-one;

- 1-(1-ethyl-propyl)-4,7-dimethyl-5-(2,4,6-trimethyl-phenoxy)-1,4-dihydro-2H-pyrido[3,4-b]pyrazin-3-one;
- 1-(1-ethyl-propyl)-4,7-dimethyl-5-(2,4,6-trimethyl-phenoxy)-1,2,3,4-tetrahydro-pyrido[3,4-b]pyrazine;
- 5 1-(1-ethyl-propyl)-7-methyl-5-(2,4,6-trimethyl-phenoxy)-1,2,3,4-tetrahydro-pyrido[3,4-b]pyrazine;
- 1-(1-ethyl-propyl)-7-methyl-2-oxo-5-(2,4,6-trimethyl-phenoxy)-1,2,3,4-tetrahydro-[1,6]naphthyridine-3-carboxylic acid methyl ester;
- 10 1-(1-ethyl-propyl)-7-methyl-2-oxo-5-(2,4,6-trimethyl-phenoxy)-1,2,3,4-tetrahydro-[1,6]naphthyridine-3-carboxylic acid isopropyl ester;
- 1-(1-ethyl-propyl)-7-methyl-5-(2,4,6-trimethyl-phenoxy)-3,4-dihydro-1H-[1,6]naphthyridin-2-one;
- 1-(1-ethyl-propyl)-7-methyl-5-(2,4,6-trimethyl-phenoxy)-1,2,3,4-tetrahydro-[1,6]naphthyridine;
- 15 1-(1-ethyl-propyl)-7-methyl-5-(2,4,6-trimethyl-phenoxy)-1,4-dihydro-2H-3-oxa-1,6-diaza-naphthalene;
- 1-(1-ethyl-propyl)-4,7-dimethyl-5-(2,4,6-trimethyl-phenoxy)-1,4-dihydro-2H-3-oxa-1,6-diaza-naphthalene;
- 1-(1-ethyl-propyl)-3,7-dimethyl-5-(2,4,6-trimethyl-phenoxy)-3,4-dihydro-20 1H-3-oxa-[1,6]-naphthyridin-2-one;
- 1-(1-ethyl-propyl)-3,3,6-trimethyl-4-(2,4,6-trimethyl-phenoxy)-2,3-dihydro-1H-pyrrolo[3,2-c]pyridine;
- 7-(1-ethyl-propoxy)-5-methyl-3-(2,4,6-trimethyl-phenyl)-pyrazolo[1,5-a]pyrimidine;
- 25 [2,5-dimethyl-3-(2,4,6-trimethyl-phenyl)-pyrazolo[1,5-a]pyrimidin-7-yl]-(1-ethyl-propyl)-amine;
- (1-ethyl-propyl)-[5-methyl-3-(2,4,6-trimethyl-phenyl)-pyrazolo[1,5-a]pyrimidin-7-yl]-amine;
- 7-(1-ethyl-propoxy)-2,5-dimethyl-3-(2,4,6-trimethyl-phenyl)-pyrazolo[1,5-a]pyrimidine;
- 30 a]pyrimidine;
- [2,5-dimethyl-3-(2,4,6-trimethyl-phenyl)-pyrazolo[1,5-a]pyrimidin-7-yl]-ethyl-propyl-amine;
- [6-bromo-5-bromomethyl-3-(2,4,6-trimethyl-phenyl)-3H-[1,2,3]triazolo[4,5-b]pyridin-7-yl]-(1-ethyl-propyl)-amine;

- (1-ethyl-propyl)-[5-methyl-3-(2,4,6-trimethyl-phenyl)-3H-[1,2,3]triazolo[4,5-b]pyridin-7-yl]-amine;
- [6-bromo-5-methyl-3-(2,4,6-trimethyl-phenyl)-3H-[1,2,3]triazolo[4,5-b]pyridin-7-yl]-(1-ethyl-propyl)-methyl-amine;
- 5 7-(1-ethyl-propoxy)-5-methyl-3-(2,4,6-trimethyl-phenyl)-3H-[1,2,3]triazolo[4,5-b]pyridine;
- 4-(1-ethyl-propoxy)-2,5-dimethyl-7-(2,4,6-trimethyl-phenyl)-5H-pyrrolo[3,2-d]pyrimidine;
- (+)-2,5-dimethyl-4-(tetrahydro-furan-3-yloxy)-7-(2,4,6-trimethyl-phenyl)-5H-pyrrolo-[3,2-d]pyrimidine;
- 10 2,5-dimethyl-4-(S)-(tetrahydro-furan-3-yloxy)-7-(2,4,6-trimethyl-phenyl)-5H-pyrrolo-[3,2-d]pyrimidine;
- 2,5-dimethyl-4-(1-propyl-butoxy)-7-(2,4,6-trimethyl-phenyl)-5H-pyrrolo[3,2-d]pyrimidine;
- 15 4-sec-butylsulfanyl-2,5-dimethyl-7-(2,4,6-trimethyl-phenyl)-5H-pyrrolo[3,2-d]pyrimidine;
- 4-(butyl-ethyl-amino)-2,6-dimethyl-8-(2,4,6-trimethyl-phenyl)-5,8-dihydro-6H-pyrido[2,3-d]pyrimidin-7-one;
- 8-(1-ethyl-propoxy)-6-methyl-4-(2,4,6-trimethyl-phenyl)-3,4-dihydro-1H-pyrido[2,3-b] pyrazin-2-one;
- 20 8-(1-ethyl-propoxy)-6-methyl-4-(2,4,6-trimethyl-phenyl)-1,2,3,4-tetrahydro-pyrido [2,3-b]pyrazine;
- 4-(1-ethyl-propoxy)-2-methyl-8-(2,4,6-trimethyl-phenyl)-quinoline;
- 5-(1-ethyl-propoxy)-7-methyl-1-(2,4,6-trimethyl-phenyl)-1,4-dihydro-2H-3-oxa-1,8-diaza-naphthalene;
- 25 5-(1-ethyl-propoxy)-7-methyl-1-(2,4,6-trimethyl-phenyl)-1,2-dihydro-3-oxa-1,8-diaza-naphthalen-4-one;
- 8-(1-ethyl-propoxy)-1,6-dimethyl-4-(2,4,6-trimethyl-phenyl)-1,2,3,4-tetrahydro-pyrido[2,3-b]pyrazine;
- 30 (1-ethyl-propyl)-[2-methyl-8-(2,4,6-trimethyl-phenyl)-quinolin-4-yl]-amine;
- 4-(butyl-ethyl-amino)-2,6-dimethyl-8-(2,6-dimethyl-4-bromo-phenyl)-5,8-dihydro-6H-pyrido[2,3-d]pyrimidin-7-one;
- 4-(butyl-ethyl-amino)-2-methyl-8-(2,6-dimethyl-4-bromo-phenyl)-5,8-dihydro-6H-pyrido[2,3-d]pyrimidin-7-one;

- 4-(1-ethyl-propoxy)-2-methyl-8-(2,6-dimethyl-4-bromo-phenyl)-5,8-dihydro-6H-pyrido[2,3-d]pyrimidin-7-one;
- (butyl-ethyl)-[2-methyl-8-(2,6-dimethyl-4-bromo-phenyl)-5,6,7,8-tetrahydro-pyrido[2,3-d]pyrimidin-4-yl]-amine;
- 5 (propyl-ethyl)-[2-methyl-8-(2,6-dimethyl-4-bromo-phenyl)-5,6,7,8-tetrahydro-pyrido[2,3-d]pyrimidin-4-yl]-amine;
- (diethyl)-[2-methyl-8-(2,6-dimethyl-4-bromo-phenyl)-5,6,7,8-tetrahydro-pyrido [2,3-d]pyrimidin-4-yl]-amine;
- (1-ethyl-propyl)-[2-methyl-8-(2,6-dimethyl-4-bromo-phenyl)-5,6,7,8-tetrahydro- pyrido[2,3-d]pyrimidin-4-yl]-amine;
- 10 (1-ethyl-propoxy)-2-methyl-8-(2,6-dimethyl-4-bromo-phenyl)-5,6,7,8-tetrahydro- pyrido[2,3-d]pyrimidine;
- 4-(butyl-ethyl-amino)-2-methyl-8-(2,4,6-trimethyl-phenyl)-5,8-dihydro-6H-pyrido[2,3-d]pyrimidin-7-one;
- 15 4-(1-ethyl-propoxy)-2-methyl-8-(2,4,6-trimethyl-phenyl)-5,8-dihydro-6H-pyrido [2,3-d]pyrimidin-7-one;
- (butyl-ethyl)-[2-methyl-8-(2,4,6-trimethyl-phenyl)-5,6,7,8-tetrahydro-pyrido[2,3-d] pyrimidin-4-yl]-amine;
- (propyl-ethyl)-[2-methyl-8-(2,4,6-trimethyl-phenyl)-5,6,7,8-tetrahydro-pyrido- [2,3-d] pyrimidin-4-yl]-amine;
- 20 (diethyl)-[2-methyl-8-(2,4,6-trimethyl-phenyl)-5,6,7,8-tetrahydro-pyrido[2,3-d] pyrimidin-4-yl]-amine;
- (1-ethyl-propyl)-[2-methyl-8-(2,4,6-trimethyl-phenyl)-5,6,7,8-tetrahydro-pyrido[2,3-d] pyrimidin-4-yl]-amine;
- 25 (1-ethyl-propoxy)-2-methyl-8-(2,4,6-trimethyl-phenyl)-5,6,7,8-tetrahydro-pyrido[2,3-d] pyrimidine;
- 8-(1-ethyl-propoxy)-6-methyl-4-(2,6-dimethyl-4-bromo-phenyl)-3,4-dihydro-1H-pyrido [2,3-b]pyrazin-2-one;
- 8-(1-ethyl-propoxy)-6-methyl-4-(2,6-dimethyl-4-bromo-phenyl)-1,2,3,4-tetrahydro- pyrido[2,3-b]pyrazine;
- 30 4-(1-ethyl-propoxy)-2-methyl-8-(2,6-dimethyl-4-bromo-phenyl)-quinoline;
- 5-(1-ethyl-propoxy)-7-methyl-1-(2,6-dimethyl-4-bromo-phenyl)-1,4-dihydro-2H-3-oxa-1,8-diaza-naphthalene;

- 5-(1-ethyl-propoxy)-7-methyl-1-(2,6-dimethyl-4-bromo-phenyl)-1,2-dihydro-3-oxa-1,8-diaza-naphthalen-4-one;
- 8-(1-ethyl-propoxy)-1,6-dimethyl-4-(2,6-dimethyl-4-bromo-phenyl)-1,2,3,4-tetrahydro-pyrido[2,3-b]pyrazine;
- 5 (1-ethyl-propyl)-[2-methyl-8-(2,6-dimethyl-4-bromo-phenyl)-quinolin-4-yl]-amine;
- 4-(butyl-ethyl-amino)-2,6-dimethyl-8-(2,6-dimethyl-4-chloro-phenyl)-5,8-dihydro-6H-pyrido[2,3-d]pyrimidin-7-one;
- 8-(1-ethyl-propoxy)-6-methyl-4-(2,6-dimethyl-4-chloro-phenyl)-3,4-dihydro-1H-pyrido[2,3-b]pyrazin-2-one;
- 10 8-(1-ethyl-propoxy)-6-methyl-4-(2,6-dimethyl-4-chloro-phenyl)-1,2,3,4-tetrahydro- pyrido[2,3-b]pyrazine;
- 4-(1-ethyl-propoxy)-2-methyl-8-(2,6-dimethyl-4-chloro-phenyl)-quinoline;
- 5-(1-ethyl-propoxy)-7-methyl-1-(2,6-dimethyl-4-chloro-phenyl)-1,4-dihydro-
- 15 2H-3-oxa-1,8-diaza-naphthalene;
- 5-(1-ethyl-propoxy)-7-methyl-1-(2,6-dimethyl-4-chloro-phenyl)-1,2-dihydro-3-oxa-1,8-diaza-naphthalen-4-one;
- 8-(1-ethyl-propoxy)-1,6-dimethyl-4-(2,6-dimethyl-4-chloro-phenyl)-1,2,3,4-tetrahydro-pyrido[2,3-b]pyrazine;
- 20 (1-ethyl-propyl)-[2-methyl-8-(2,6-dimethyl-4-chloro-phenyl)-quinolin-4-yl]-amine;
- 8-(1-hydroxymethyl-propoxy)-6-methyl-4-(2,4,6-trimethyl-phenyl)-3,4-dihydro-1H-pyrido[2,3-b]pyrazin-2-one;
- 8-(1-hydroxymethyl-propylamino)-6-methyl-4-(2,4,6-trimethyl-phenyl)-3,4-
- 25 dihydro-1H-pyrido[2,3-b]pyrazin-2-one;
- 8-(1-ethyl-propylamino)-6-methyl-4-(2,4,6-trimethyl-phenyl)-3,4-dihydro-1H-pyrido[2,3-b]pyrazin-2-one;
- 8-diethylamino-6-methyl-4-(2,4,6-trimethyl-phenyl)-3,4-dihydro-1H-pyrido-[2,3-b] pyrazin-2-one;
- 30 8-(ethyl-propyl-amino)-6-methyl-4-(2,4,6-trimethyl-phenyl)-3,4-dihydro-1H-pyrido[2,3-b]pyrazin-2-one;
- 8-(butyl-ethyl-amino)-6-methyl-4-(2,4,6-trimethyl-phenyl)-3,4-dihydro-1H-pyrido [2,3-b]pyrazin-2-one;

- 8-(1-hydroxymethyl-propoxy)-6-methyl-4-(2,4,6-trimethyl-phenyl)-1,2,3,4-tetrahydro-pyrido[2,3-b]pyrazine;
- 8-(1-hydroxymethyl-propylamino)-6-methyl-4-(2,4,6-trimethyl-phenyl)-1,2,3,4-tetrahydro-pyrido[2,3-b]pyrazine;
- 5 8-(1-ethyl-propylamino)-6-methyl-4-(2,4,6-trimethyl-phenyl)-1,2,3,4-tetrahydro-pyrido[2,3-b]pyrazine;
- 8-diethylamino-6-methyl-4-(2,4,6-trimethyl-phenyl)-1,2,3,4-tetrahydro-pyrido[2,3-b]pyrazine;
- 8-(ethyl-propyl-amino)-6-methyl-4-(2,4,6-trimethyl-phenyl)-1,2,3,4-tetrahydro-pyrido[2,3-b]pyrazine;
- 10 8-(butyl-ethyl-amino)-6-methyl-4-(2,4,6-trimethyl-phenyl)-1,2,3,4-tetrahydro-pyrido[2,3-b]pyrazine;
- 4-(1-hydroxymethyl-propoxy)-2-methyl-8-(2,4,6-trimethyl-phenyl)-quinoline;
- 4-(1-hydroxymethyl-propylamino)-2-methyl-8-(2,4,6-trimethyl-phenyl)-quinoline;
- 15 4-(1-ethyl-propylamino)-2-methyl-8-(2,4,6-trimethyl-phenyl)-quinoline;
- 4-diethylamino-2-methyl-8-(2,4,6-trimethyl-phenyl)-quinoline;
- 4-(ethyl-propyl-amino)-2-methyl-8-(2,4,6-trimethyl-phenyl)-quinoline;
- 4-(butyl-ethyl-amino)-2-methyl-8-(2,4,6-trimethyl-phenyl)-quinoline;
- 20 5-(1-hydroxymethyl-propoxy)-7-methyl-1-(2,4,6-trimethyl-phenyl)-1,4-dihydro-2H-3-oxa-1,8-diaza-naphthalene;
- 5-(1-hydroxymethyl-propylamino)-7-methyl-1-(2,4,6-trimethyl-phenyl)-1,4-dihydro-2H-3-oxa-1,8-diaza-naphthalene;
- 5-(1-ethyl-propylamino)-7-methyl-1-(2,4,6-trimethyl-phenyl)-1,4-dihydro-2H-3-oxa-1,8-diaza-naphthalene;
- 25 5-diethylamino-5-methyl-1-(2,4,6-trimethyl-phenyl)-1,4-dihydro-2H-3-oxa-1,8-diaza-naphthalene;
- 5-(ethyl-propyl-amino)-7-methyl-1-(2,4,6-trimethyl-phenyl)-1,4-dihydro-2H-3-oxa-1,8-diaza-naphthalene;
- 30 8-(butyl-ethyl-amino)-6-methyl-4-(2,4,6-trimethyl-phenyl)-1,4-dihydro-2H-3-oxa-1,8-diaza-naphthalene;
- 4-(2,4-dichlorophenyl)-5-methyl-2-[N-(1-(methoxymethyl)-1-(naphth-2-yl)methyl)-N-propylamino]thiazole;

- oxalate of 4-(2,4-dichlorophenyl)-5-methyl-2-[N-(6-methoxyisoquinol-5-yl)-N-propylamino]thiazole;
- oxalate of 4-(2-chloro-4-methoxyphenyl)-5-methyl-2-[N-(6-methylisoquinol-5-yl)-N-propylamino]thiazole;
- 5 4-(2-chloro-4-methoxyphenyl)-5-methyl-2-[N-(1-methoxycarbonylmethylindol-5-yl)-N-propylamino]thiazole;
- oxalate of 4-(2-chloro-4-methoxyphenyl)-5-methyl-2-[N-(6-methoxyisoquinol-5-yl)-N-propylamino]thiazole;
- oxalate of 4-(2-chloro-4-methoxyphenyl)-5-methyl-2-[N-(6-chloroisoquinol-5-yl)-N-propylamino]thiazole;
- 10 -yl)-N-propylamino]thiazole;
- oxalate of 4-(2-chloro-4-methoxyphenyl)-5-methyl-2-[N-(6-methoxyisoquinol-5-yl)-N-propylamino]thiazole;
- 4-(2-chloro-4-methoxyphenyl)-5-methyl-2-[N-1-methoxynaphth-2-yl)-N-propylamino]thiazole;
- 15 oxalate of 4-(2-chloro-4-trifluoromethylphenyl)-5-methyl-2-[N-6-methoxyisoquinol-5-yl)-N-propylamino]thiazole;
- chlorhydrate of 4-(2-chloro-4-methoxyphenyl)-5-methyl-2-[N-(2-ethoxynaphth-1-yl)-N-propylamino]thiazole;
- chlorhydrate of 4-(2-chloro-4-methoxyphenyl)-5-methyl-2-[N-(2,3-dimethylnaphth-1-yl)-N-propylamino]thiazole;
- 20 chlorhydrate of 4-(2-chloro-4-methoxyphenyl)-5-methyl-2-[N-(6-bromo-2-methoxynaphth-1-yl)-N-propylamino]thiazole;
- chlorhydrate of 4-(2-chloro-4-methoxyphenyl)-5-methyl-2-[N-(2,6-dimethylnaphth-1-yl)-N-propylamino]thiazole;
- 25 chlorhydrate of 4-(2-chloro-4-methoxyphenyl)-5-methyl-2-[N-(1-(methoxymethyl)-1-(naphth-2-yl)methyl)-N-propylamino]thiazole;
- chlorhydrate of 4-(2-chloro-4-methoxyphenyl)-5-methyl-2-[N-(1-(cyclopropyl)-1-(naphth-2-yl)methyl)-N-propylamino]thiazole;
- 3-(2,4-dichlorophenyl)-5-methyl-7-(N-propyl-N-cyclopropanemethylamino)-pyrazolo[2,3-a]pyrimidine;
- 30 3-(2,4-dichlorophenyl)-5-methyl-7-(N-allyl-N-cyclopropanemethylamino)-pyrazolo[2,3-a]pyrimidine;
- 2-methylthio-3-(2,4-dichlorophenyl)-5-methyl-7-(N,N-diallylamino)-pyrazolo[2,3-a]pyrimidine;

2-methylthio-3-(2,4-dichlorophenyl)-5-methyl-7-(N-butyl-N-cyclopropane-methyl-amino)pyrazolo[2,3-a]pyrimidine;

2-methylthio-3-(2,4-dichlorophenyl)-5-methyl-7-(N-propyl-N-cyclopropane-methyl-amino)pyrazolo[2,3-a]pyrimidine;

5 2-methyl-3-(4-chlorophenyl)-5-methyl-7-(N,N-dipropylamino)-pyrazolo[2,3-a]pyrimidine;

3-[6-(dimethylamino)-3-pyridinyl-2,5-dimethyl-N,N-dipropylpyrazolo[2,3-a]pyrimidin-7-amine;

10 3-[6-(dimethylamino)-4-methyl-3-pyridinyl]-2,5-dimethyl-N,N-dipropylpyrazolo[2,3-a]pyrimidine-7-amine;

3-(2,4-dimethoxyphenyl)-2,5-dimethyl-7-(N-propyl-N-methoxyethylamino)-pyrazolo(2,3-a)pyrimidine;

7-(N-diethylamino)-2,5-dimethyl-3-(2-methyl-4-methoxyphenyl)-[1,5-a]-pyrazolopyrimidine;

15 7-(N-(3-cyanopropyl)-N-propylamino-2,5-dimethyl-3-(2,4-dimethylphenyl)-[1,5-a]-pyrazolopyrimidine;

[3,6-dimethyl-2-(2,4,6-trimethyl-phenoxy)-pyridin-4-yl]-(1-ethyl-propyl)-amine;

[2-(4-chloro-2,6-dimethyl-phenoxy)-3,6-dimethyl-pyridin-4-yl]-(1-ethyl-propyl)-amine;

20 cyclopropylmethyl-[3-(2,4-dimethyl-phenyl)-2,5-dimethyl-pyrazolo[1,5-a]pyrimidin-7-yl]-propyl-amine;

cyclopropylmethyl-[3-(2-methyl-4-chloro-phenyl)-2,5-dimethyl-pyrazolo[1,5-a]pyrimidin-7-yl]-propyl-amine;

25 cyclopropylmethyl-[3-(2,4-di-chloro-phenyl)-2,5-dimethyl-pyrazolo[1,5-a]pyrimidin-7-yl]-propyl-amine;

[3-(2-methyl-4-chloro-phenyl)-2,5-dimethyl-pyrazolo[1,5-a]pyrimidin-7-yl]-di-propyl-amine;

[2,5-dimethyl-3-(2,4-dimethyl-phenyl)-pyrazolo[1,5-a]pyrimidin-7-yl]-(1-ethyl-propyl)-amine;

30 [2,5-dimethyl-3-(2,4-dichloro-phenyl)-pyrazolo[1,5-a]pyrimidin-7-yl]-(1-ethyl-propyl)-amine;

4-(1-ethyl-propylamino)-6-methyl-2-(2,4,6-trimethyl-phenoxy)-nicotinic acid methyl ester;

3-[6-(dimethylamino)-4-methyl-3-pyridinyl]-2,5-dimethyl-N-propyl-N-cyclopropylmethyl-pyrazolo[2,3-a]pyrimidin-7-amine; and

3-[6-(dimethylamino)-4-methyl-3-pyridinyl]-2,5-dimethyl-N-ethyl-N-cyclopropylmethyl-pyrazolo[2,3-a]pyrimidin-7-amine.

5

14. A pharmaceutical composition according to claim 13 wherein said corticotropin releasing factor antagonist is a compound selected from the group consisting of:

- 10 4-(1-ethyl-propoxy)-3,6-dimethyl-2-(2,4,6-trimethylphenoxy)-pyridine;
4-(1-ethylpropoxy)-2,5-dimethyl-6-(2,4,6-trimethylphenoxy)-pyrimidine;
[4-(1-ethyl-propoxy)-3,6-dimethyl-pyridin-2-yl]-(2,4,6-trimethylphenyl)-amine;
3-[(4-methyl-benzyl)-[3,6-dimethyl-1-(2,4,6-trimethylphenyl)-1H-pyrazolo[3,4-
d]pyrimidin-4-yl]-amino}-propan-1-ol;
propyl-ethyl-[3,6-dimethyl-1-(2,4,6-trimethylphenyl)-1H-pyrazolo[3,4-
15 d]pyrimidin-4-yl]-amine;
ethyl-n-propyl-[2,5-dimethyl-7-(2,4,6-trimethylphenyl)-7H-pyrrolo[2,3-
d]pyrimidin-4-yl]amine;
2-{N-n-butyl-N-[2,5-dimethyl-7-(2,4,6-trimethylphenyl)-7H-pyrrolo[2,3-
d]pyrimidin-4-yl]amino}-ethanol;
20 [3,6-dimethyl-1-(2,4,6-trimethylphenyl)-1H-pyrazolo[3,4,b]pyridin-4-yl]-(1-
methoxymethylpropyl)-amine;
4-(1-ethylpropoxy)-2,5-dimethyl-7-(2,4,6-trimethylphenyl)-7H-pyrrolo[2,3-
b]pyridine;
2,5,6-trimethyl-7-(1-propylbutyl)-4-(2,4,6-trimethylphenoxy)-7H-pyrrolo[2,3-
25 d]pyrimidine;
1-(1-ethylpropyl)-6-methyl-4-(2,4,6-trimethylphenoxy)-1,3-dihydro-imidazo[4,5-
c]pyridin-2-one;
1-(1-ethyl-propyl)-4,7-dimethyl-5-(2,4,6-trimethyl-phenoxy)-1,4-dihydro-
2H-pyrido[3,4-b]pyrazin-3-one;
30 1-(1-ethyl-propyl)-4,7-dimethyl-5-(2,4,6-trimethyl-phenoxy)-1,2,3,4-
tetrahydro-pyrido[3,4-b]pyrazine;
1-(1-ethyl-propyl)-7-methyl-2-oxo-5-(2,4,6-trimethyl-phenoxy)-1,2,3,4-tetra-
hydro-[1,6]naphthyridine-3-carboxylic acid isopropyl ester;

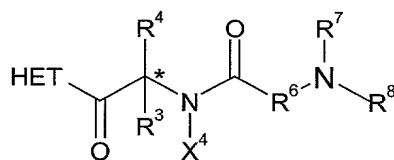
- 1-(1-ethyl-propyl)-7-methyl-5-(2,4,6-trimethyl-phenoxy)-1,4-dihydro-2H-3-oxa-1,6-diaza-naphthalene;
- (1-ethyl-propyl)-[5-methyl-3-(2,4,6-trimethyl-phenyl)-pyrazolo[1,5-a]pyrimidin-7-yl]-amine;
- 5 7-(1-ethyl-propoxy)-2,5-dimethyl-3-(2,4,6-trimethyl-phenyl)-pyrazolo[1,5-a]pyrimidine;
- 4-(1-ethyl-propoxy)-2,5-dimethyl-7-(2,4,6-trimethyl-phenyl)-5H-pyrrolo[3,2-d]pyrimidine;
- 4-(butyl-ethyl-amino)-2,6-dimethyl-8-(2,4,6-trimethyl-phenyl)-5,8-dihydro-6H-pyrido[2,3-d]pyrimidin-7-one;
- 10 8-(1-ethyl-propoxy)-6-methyl-4-(2,4,6-trimethyl-phenyl)-1,2,3,4-tetrahydro-pyrido [2,3-b]pyrazine;
- 4-(1-ethyl-propoxy)-2-methyl-8-(2,4,6-trimethyl-phenyl)-quinoline;
- (1-ethyl-propyl)-[2-methyl-8-(2,4,6-trimethyl-phenyl)-quinolin-4-yl]-amine;
- 15 (propyl-ethyl)-[2-methyl-8-(2,4,6-trimethyl-phenyl)-5,6,7,8-tetrahydro-pyrido[2,3-d] pyrimidin-4-yl]-amine;
- (1-ethyl-propoxy)-2-methyl-8-(2,4,6-trimethyl-phenyl)-5,6,7,8-tetrahydro-pyrido[2,3-d] pyrimidine;
- 8-(1-hydroxymethyl-propylamino)-6-methyl-4-(2,4,6-trimethyl-phenyl)-3,4-dihydro-1H-pyrido[2,3-b]pyrazin-2-one;
- 20 4-(1-hydroxymethyl-propylamino)-2-methyl-8-(2,4,6-trimethyl-phenyl)-quinoline;
- 5-(1-hydroxymethyl-propylamino)-7-methyl-1-(2,4,6-trimethyl-phenyl)-1,4-dihydro-2H-3-oxa-1,8-diaza-naphthalene;
- 25 [3,6-dimethyl-2-(2,4,6-trimethyl-phenoxy)-pyridin-4-yl]-(1-ethyl-propyl)-amine;
- cyclopropylmethyl-[3-(2,4-dimethyl-phenyl)-2,5-dimethyl-pyrazolo[1,5-a]pyrimidin-7-yl]-propyl-amine;
- [2,5-dimethyl-3-(2,4-dimethyl-phenyl)-pyrazolo[1,5-a]pyrimidin-7-yl]-(1-ethyl-propyl)-amine;
- 30 3-[6-(dimethylamino)-3-pyridinyl-2,5-dimethyl-N,N-dipropylpyrazolo[2,3-a]pyrimidin-7-amine;
- 3-[6-(dimethylamino)-4-methyl-3-pyridinyl]-2,5-dimethyl-N,N-dipropyl-pyrazolo[2,3-a]pyrimidine-7-amine;

3-(2,4-dimethoxyphenyl)-2,5-dimethyl-7-(N-propyl-N-methoxyethylamino)-pyrazolo(2,3-a)pyrimidine;

7-(N-diethylamino)-2,5-dimethyl-3-(2-methyl-4-methoxyphenyl-[1,5-a]-pyrazolopyrimidine; and

5 7-(N-(3-cyanopropyl)-N-propylamino-2,5-dimethyl-3-(2,4-dimethylphenyl)-[1,5-a]-pyrazolopyrimidine.

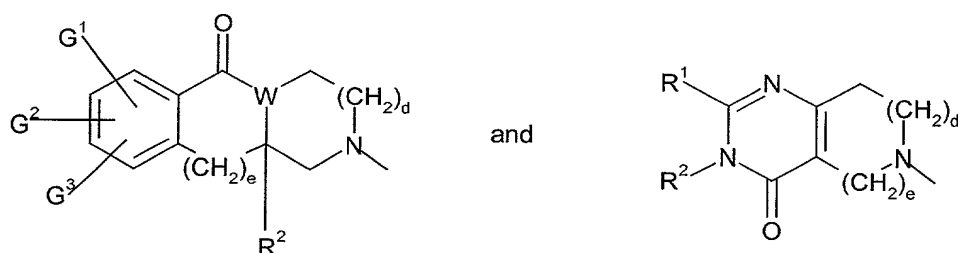
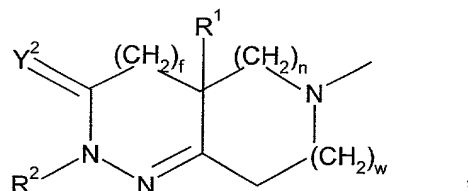
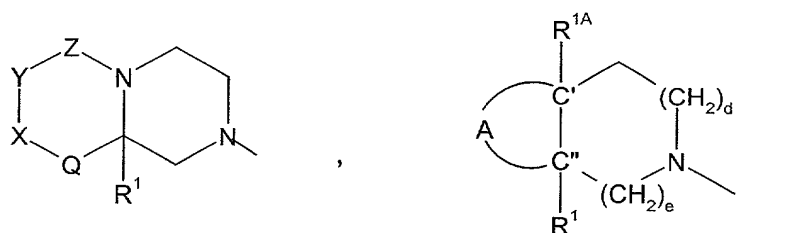
15. A pharmaceutical composition according to claim 1 wherein said growth hormone secretagogue is a compound of formula IV:



IV

or a stereoisomeric mixture thereof, a diastereomerically enriched, diastereomerically pure, enantiomerically enriched, or enantiomerically pure isomer thereof, or a prodrug of such compound, mixture, or isomer thereof, or a pharmaceutically acceptable salt of the compound, mixture, isomer, or prodrug, wherein:

HET is a heterocyclic moiety selected from the group consisting of



d is 0, 1, or 2;

e is 1 or 2;

f is 0 or 1;

5 n and w are 0, 1, or 2, provided that n and w cannot both be 0 at the same time;

Y² is oxygen or sulfur;

A is a divalent radical, wherein the left hand side of the radical as shown below is connected to C" and the right hand side of the radical as shown below is

10 connected to C', selected from the group consisting of -NR²-CO-NR²-, -NR²-SO₂-NR²-, -O-CO-NR²-, -NR²-CO₂-, -CO-NR²-CO-, -CO-NR²-C(R⁹R¹⁰)-, -C(R⁹R¹⁰)-NR²-CO-, -C(R⁹R¹⁰)-C(R⁹R¹⁰)-C(R⁹R¹⁰)-, -SO₂-C(R⁹R¹⁰)-C(R⁹R¹⁰)-, -C(R⁹R¹⁰)-O-CO-, -C(R⁹R¹⁰)-O-C(R⁹R¹⁰)-, -NR²-CO-C(R⁹R¹⁰)-, -O-CO-C(R⁹R¹⁰)-, -C(R⁹R¹⁰)-CO-NR²-, -CO-NR²-CO-, -C(R⁹R¹⁰)-CO₂-, -CO-NR²-C(R⁹R¹⁰)-C(R⁹R¹⁰)-,

15 -CO₂-C(R⁹R¹⁰)-, -C(R⁹R¹⁰)-C(R⁹R¹⁰)-C(R⁹R¹⁰)-C(R⁹R¹⁰)-, -SO₂-NR²-C(R⁹R¹⁰)-C(R⁹R¹⁰)-, -C(R⁹R¹⁰)-C(R⁹R¹⁰)-NR²-CO-, -C(R⁹R¹⁰)-C(R⁹R¹⁰)-O-CO-, -NR²-CO-C(R⁹R¹⁰)-C(R⁹R¹⁰)-, -NR²-SO₂-C(R⁹R¹⁰)-C(R⁹R¹⁰)-, -O-CO-C(R⁹R¹⁰)-C(R⁹R¹⁰)-, -C(R⁹R¹⁰)-C(R⁹R¹⁰)-CO-NR²-, -C(R⁹R¹⁰)-C(R⁹R¹⁰)-CO-, -C(R⁹R¹⁰)-NR²-CO₂-, -C(R⁹R¹⁰)-O-CO-NR²-, -C(R⁹R¹⁰)-NR²-CO-NR²-, -NR²-CO₂-C(R⁹R¹⁰)-, -NR²-CO-NR²-

$C(R^9R^{10})-$, $-NR^2-SO_2-NR^2-C(R^9R^{10})-$, $-O-CO-NR^2-C(R^9R^{10})-$, $-CO-N=C(R^{11})-NR^2-$,
 $-CO-NR^2-C(R^{11})=N-$, $-C(R^9R^{10})-NR^{12}-C(R^9R^{10})-$, $-NR^{12}-C(R^9R^{10})-$, $-NR^{12}-C(R^9R^{10})-$
 $C(R^9R^{10})-$, $-CO_2-C(R^9R^{10})-C(R^9R^{10})-$, $-NR^2-C(R^{11})=N-CO-$, $-C(R^9R^{10})-C(R^9R^{10})-N(R^{12})-$,
 $-C(R^9R^{10})-NR^{12}-$, $-N=C(R^{11})-NR^2-CO-$, $-C(R^9R^{10})-C(R^9R^{10})-NR^2-SO_2-$, $-C(R^9R^{10})-$
5 $C(R^9R^{10})-SO_2-NR^2-$, $-C(R^9R^{10})-C(R^9R^{10})-CO_2-$, $-C(R^9R^{10})-SO_2-C(R^9R^{10})-$, $-C(R^9R^{10})-$
 $C(R^9R^{10})-SO_2-$, $-O-C(R^9R^{10})-C(R^9R^{10})-$, $-C(R^9R^{10})-C(R^9R^{10})-O-$, $-C(R^9R^{10})-CO-$
 $C(R^9R^{10})-$, $-CO-C(R^9R^{10})-C(R^9R^{10})-$, and $-C(R^9R^{10})-NR^2-SO_2-NR^2-$;

Q is a covalent bond or CH_2 ;

W is CH or N;

10 X is CR^9R^{10} , $C=CH_2$, or $C=O$;

Y is CR^9R^{10} , O, or NR^2 ;

Z is $C=O$, $C=S$, or SO_2 ;

G^1 is hydrogen, halo, hydroxy, nitro, amino, cyano, phenyl, carboxyl, $-CONH_2$,
 $-C_1-C_4$ alkyl optionally independently substituted with one or more phenyl, one or
15 more halogen, or one or more hydroxy groups, $-C_1-C_4$ alkoxy optionally independently
substituted with one or more phenyl, one or more halogen, or one or more hydroxy
groups, $-C_1-C_4$ alkylthio, phenoxy, $-CO_2-(C_1-C_4$ alkyl), N,N-di-(C_1-C_4 alkylamino), $-C_2-$
 C_6 alkenyl optionally independently substituted with one or more phenyl, one or more
halogen, or one or more hydroxy groups, $-C_2-C_6$ alkynyl optionally independently
20 substituted with one or more phenyl, one or more halogen, or one or more hydroxy
groups, $-C_3-C_6$ cycloalkyl optionally independently substituted with one or more C_1-C_4
alkyl groups, one or more halogen, or one or more hydroxy groups, $-C_1-C_4$ alkylamino
carbonyl, or di- C_1-C_4 alkylamino) carbonyl;

G^2 and G^3 are each independently selected from the group consisting of
25 hydrogen, halo, hydroxy, $-C_1-C_4$ alkyl optionally independently substituted with one to
three halo groups, and $-C_1-C_4$ alkoxy optionally independently substituted with one to
three halo groups;

R^1 is hydrogen, $-CN$, $-(CH_2)_qNX^6COX^6$, $-(CH_2)_qNX^6CO(CH_2)_tA^1$,
 $-(CH_2)_qNX^6SO_2(CH_2)_tA^1$, $-(CH_2)_qNX^6SO_2X^6$, $-(CH_2)_qNX^6CONX^6(CH_2)_tA^1$,
30 $-(CH_2)_qNX^6CONX^6X^6$, $-(CH_2)_qCONX^6X^6$, $-(CH_2)_qCONX^6(CH_2)_tA^1$, $-(CH_2)_qCO_2X^6$,
 $-(CH_2)_qCO_2(CH_2)_tA^1$, $-(CH_2)_qOX^6$, $-(CH_2)_qOCOX^6$, $-(CH_2)_qOCO(CH_2)_tA^1$,
 $-(CH_2)_qOCONX^6(CH_2)_tA^1$, $-(CH_2)_qOCONX^6X^6$, $-(CH_2)_qCOX^6$, $-(CH_2)_qCO(CH_2)_tA^1$,
 $-(CH_2)_qNX^6CO_2X^6$, $-(CH_2)_qNX^6SO_2NX^6X^6$, $-(CH_2)_qSO_mX^6$, $-(CH_2)_qSO_m(CH_2)_tA^1$,

-C₁-C₁₀ alkyl, -(CH₂)_t-A¹, -(CH₂)_q-(C₃-C₇ cycloalkyl), -(CH₂)_q-Y¹-(C₁-C₆ alkyl), -(CH₂)_q-Y¹-(CH₂)_t-A¹, or -(CH₂)_q-Y¹-(CH₂)_t-(C₃-C₇ cycloalkyl);

wherein the alkyl and cycloalkyl groups in the definition of R¹ are optionally substituted with C₁-C₄ alkyl, hydroxy, C₁-C₄ alkoxy, carboxyl, -CONH₂, -SO_m-(C₁-C₆ alkyl), -CO₂-(C₁-C₄ alkyl) ester, 1H-tetrazol-5-yl, or 1, 2, or 3 fluoro groups;

Y¹ is O, SO_m, -CONX⁶-, -CH=CH-, -C≡C-, -NX⁶CO-, -CONX⁶-, -CO₂-, -OCONX⁶- or -OCO-;

q is 0, 1, 2, 3, or 4;

t is 0, 1, 2, or 3;

said (CH₂)_q group and (CH₂)_t group in the definition of R¹ are optionally independently substituted with hydroxy, C₁-C₄ alkoxy, carboxyl, -CONH₂, -SO_m-(C₁-C₆ alkyl), -CO₂-(C₁-C₄ alkyl) ester, 1H-tetrazol-5-yl, 1, 2, or 3 fluoro groups, or 1 or 2 C₁-C₄ alkyl groups;

R^{1A} is selected from the group consisting of hydrogen, F, Cl, Br, I, C₁-C₆ alkyl, phenyl-(C₁-C₃ alkyl), pyridyl-(C₁-C₃ alkyl), thiazolyl-(C₁-C₃ alkyl), and thienyl-(C₁-C₃ alkyl), provided that R^{1A} is not F, Cl, Br, or I when a heteroatom is vicinal to C^o;

R² is hydrogen, C₁-C₈ alkyl, -(C₀-C₃ alkyl)-(C₃-C₈ cycloalkyl), -(C₁-C₄ alkyl)-A¹, or A¹, wherein the alkyl groups and the cycloalkyl groups in the definition of R² are optionally substituted with hydroxy, -CO₂X⁶, -CONX⁶X⁶, -NX⁶X⁶, -SO_m(C₁-C₆ alkyl), -COA¹, -COX⁶, CF₃, CN, or 1, 2, or 3 independently selected halo groups;

R³ is selected from the group consisting of A¹, C₁-C₁₀ alkyl, -(C₁-C₆ alkyl)-A¹, -(C₁-C₆ alkyl)-(C₃-C₇ cycloalkyl), -(C₁-C₅ alkyl)-X¹-(C₁-C₅ alkyl), -(C₁-C₅ alkyl)-X¹-(C₀-C₅ alkyl)-A¹, and -(C₁-C₅ alkyl)-X¹-(C₁-C₅ alkyl)-(C₃-C₇ cycloalkyl);

wherein the alkyl groups in the definition of R³ are optionally substituted with -SO_m(C₁-C₆ alkyl), -CO₂X³, 1, 2, 3, 4, or 5 independently selected halo groups, or 1, 2, or 3 independently selected -OX³ groups;

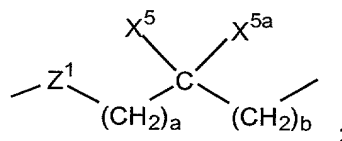
X¹ is O, SO_m, -NX²CO-, -CONX²-, -OCO-, -CO₂-, -CX²=CX²-, -NX²CO₂-, -OCONX²-, or -C≡C-;

R⁴ is hydrogen, C₁-C₆ alkyl, or C₃-C₇ cycloalkyl, or R⁴ taken together with R³ and the carbon atom to which they are attached form C₅-C₇ cycloalkyl, C₅-C₇ cycloalkenyl, a partially saturated or fully saturated 4- to 8-membered ring having 1 to 4 heteroatoms independently selected from the group consisting of oxygen, sulfur, and nitrogen, or a bicyclic ring system consisting of a partially saturated or fully

saturated 5- or 6-membered ring, fused to a partially saturated, fully unsaturated, or fully saturated 5- or 6-membered ring, optionally having 1 to 4 heteroatoms independently selected from the group consisting of nitrogen, sulfur, and oxygen;

5 X^4 is hydrogen or C_1-C_6 alkyl, or X^4 is taken together with R^4 and the nitrogen atom to which X^4 is attached and the carbon atom to which R^4 is attached and form a five to seven membered ring;

R^6 is a bond or is



10 wherein a and b are each independently 0, 1, 2, or 3;

X^5 and X^{5a} are each independently selected from the group consisting of hydrogen, CF_3 , A^1 , and C_1-C_6 alkyl optionally substituted with A^1 , OX^2 , $-SO_m-(C_1-C_6 \text{ alkyl})$, $-CO_2X^2$, C_3-C_7 cycloalkyl, $-NX^2X^2$, or $-CONX^2X^2$;

15 or the carbon bearing X^5 or X^{5a} forms one or two alkylene bridges with the nitrogen atom bearing R^7 and R^8 wherein each alkylene bridge contains 1 to 5 carbon atoms, provided that when one alkylene bridge is formed then only one of X^5 or X^{5a} is on the carbon atom and only one of R^7 or R^8 is on the nitrogen atom, and further provided that when two alkylene bridges are formed then X^5 and X^{5a} cannot be on the carbon atom and R^7 and R^8 cannot be on the nitrogen atom;

20 or X^5 taken together with X^{5a} and the carbon atom to which they are attached form a partially saturated or fully saturated 3- to 7-membered ring, or a partially saturated or fully saturated 4- to 8-membered ring having 1 to 4 heteroatoms independently selected from the group consisting of oxygen, sulfur, and nitrogen;

25 or X^5 taken together with X^{5a} and the carbon atom to which they are attached form a bicyclic ring system consisting of a partially saturated or fully saturated 5- or 6-membered ring, optionally having 1 or 2 heteroatoms independently selected from the group consisting of nitrogen, sulfur, and oxygen, fused to a partially saturated, fully saturated, or fully unsaturated 5- or

30

6-membered ring, optionally having 1 to 4 heteroatoms independently selected from the group consisting of nitrogen, sulfur, and oxygen;

Z^1 is a bond, O, or $N-X^2$, provided that when a and b are both 0 then Z^1 is not $N-X^2$ or O;

5 R^7 and R^8 are each independently hydrogen or C_1-C_6 alkyl optionally independently substituted with A^1 , $-CO_2-(C_1-C_6 \text{ alkyl})$, $-SO_m(C_1-C_6 \text{ alkyl})$, 1 to 5 halo groups, 1 to 3 hydroxy groups, 1 to 3 $-O-CO(C_1-C_{10} \text{ alkyl})$ groups, or 1 to 3 C_1-C_6 alkoxy groups; or

10 R^7 and R^8 can be taken together to form $-(CH_2)_r-L-(CH_2)_r-$, wherein L is CX^2X^2 , SO_m , or NX^2 ;

R^9 and R^{10} are each independently selected from the group consisting of hydrogen, fluoro, hydroxy, and C_1-C_5 alkyl optionally independently substituted with 1-5 halo groups;

15 R^{11} is selected from the group consisting of C_1-C_5 alkyl and phenyl optionally substituted with 1-3 substituents each independently selected from the group consisting of C_1-C_5 alkyl, halo, and C_1-C_5 alkoxy;

R^{12} is selected from the group consisting of C_1-C_5 alkylsulfonyl, C_1-C_5 alkanoyl, and C_1-C_5 alkyl wherein the alkyl portion is optionally independently substituted by 1-5 halo groups;

20 A^1 for each occurrence is independently selected from the group consisting of C_5-C_7 cycloalkenyl, phenyl, a partially saturated, fully saturated, or fully unsaturated 4- to 8-membered ring optionally having 1 to 4 heteroatoms independently selected from the group consisting of oxygen, sulfur, and nitrogen, and a bicyclic ring system consisting of a partially saturated, fully unsaturated, or fully saturated 5- or 6-
25 membered ring, optionally having 1 to 4 heteroatoms independently selected from the group consisting of nitrogen, sulfur, and oxygen, fused to a partially saturated, fully saturated, or fully unsaturated 5- or 6-membered ring, optionally having 1 to 4 heteroatoms independently selected from the group consisting of nitrogen, sulfur, and oxygen;

30 A^1 for each occurrence is independently optionally substituted, on one or optionally both rings if A^1 is a bicyclic ring system, with up to three substituents, each substituent independently selected from the group consisting of F, Cl, Br, I, OCF_3 , OCF_2H , CF_3 , CH_3 , OCH_3 , $-OX^6$, $-CONX^6X^6$, $-CO_2X^6$, oxo, C_1-C_6 alkyl, nitro, cyano, benzyl, $-SO_m(C_1-C_6 \text{ alkyl})$, 1H-tetrazol-5-

yl, phenyl, phenoxy, phenylalkyloxy, halophenyl, methylenedioxy, $-NX^6X^6$, $-NX^6COX^6$, $-SO_2NX^6X^6$, $-NX^6SO_2$ -phenyl, $NX^6SO_2X^6$, $-CONX^{11}X^{12}$, $-SO_2NX^{11}X^{12}$, $-NX^6SO_2X^{12}$, $-NX^6CONX^{11}X^{12}$, $-NX^6SO_2NX^{11}X^{12}$, $-NX^6COX^{12}$, imidazolyl, thiazolyl, and tetrazolyl, provided that if A^1 is optionally substituted

5 with methylenedioxy then it can only be substituted with one methylenedioxy;

wherein X^{11} is hydrogen or C_1 - C_6 alkyl optionally independently substituted with phenyl, phenoxy, C_1 - C_6 alkoxy carbonyl, $-SO_m(C_1$ - C_6 alkyl), 1 to 5 halo groups, 1 to 3 hydroxy groups, 1 to 3 C_1 - C_{10} alkanoyloxy groups, or 1 to 3 C_1 - C_6 alkoxy groups;

10 X^{12} is hydrogen, C_1 - C_6 alkyl, phenyl, thiazolyl, imidazolyl, furyl, or thienyl, provided that when X^{12} is not hydrogen, the X^{12} group is optionally substituted with one to three substituents independently selected from the group consisting of Cl, F, CH_3 , OCH_3 , OCF_3 , and CF_3 ;

15 or X^{11} and X^{12} are taken together to form $-(CH_2)_r-L^1-(CH_2)_r-$, wherein L^1 is CX^2X^2 , O, SO_m , or NX^2 ;

r for each occurrence is independently 1, 2, or 3;

20 X^2 for each occurrence is independently hydrogen, optionally substituted C_1 - C_6 alkyl, or optionally substituted C_3 - C_7 cycloalkyl, wherein the optionally substituted C_1 - C_6 alkyl and optionally substituted C_3 - C_7 cycloalkyl in the definition of X^2 are optionally independently substituted with $-SO_m(C_1$ - C_6 alkyl), $-CO_2X^3$, 1 to 5 halo groups, or 1-3 OX^3 groups;

X^3 for each occurrence is independently hydrogen or C_1 - C_6 alkyl;

25 X^6 for each occurrence is independently hydrogen, optionally substituted C_1 - C_6 alkyl, halogenated C_2 - C_6 alkyl, optionally substituted C_3 - C_7 cycloalkyl, halogenated C_3 - C_7 cycloalkyl, wherein the optionally substituted C_1 - C_6 alkyl and optionally substituted C_3 - C_7 cycloalkyl in the definition of X^6 are optionally independently mono- or di-substituted with C_1 - C_4 alkyl, hydroxy, C_1 - C_4 alkoxy, carboxyl, $CONH_2$, $-SO_m(C_1$ - C_6 alkyl), carboxylate (C_1 - C_4 alkyl) ester, or 1H-tetrazol-5-yl; or

30 when there are two X^6 groups on one atom and both X^6 are independently C_1 - C_6 alkyl, the two C_1 - C_6 alkyl groups may be optionally joined, and together with the atom to which the two X^6 groups are attached, form a 4- to 9- membered ring optionally having oxygen, sulfur, or NX^7 as a ring member, wherein X^7 is hydrogen or C_1 - C_6 alkyl optionally substituted with hydroxy;

m for each occurrence is independently 0, 1, or 2;

with the provisos that:

X^6 and X^{12} cannot be hydrogen when attached to CO or SO_2 in the form COX^6 , COX^{12} , SO_2X^6 or SO_2X^{12} ; and

5 when R^6 is a bond then L is NX^2 and each r in the definition $-(CH_2)_r-L-(CH_2)_r$ is independently 2 or 3.

16. A pharmaceutical composition according to claim 15 wherein said growth hormone secretagogue is

10 2-amino-N-(2-(3a-(R)-benzyl-2-methyl-3-oxo-2,3,3a,4,6,7-hexahydro-pyrazolo-[4,3-c]pyridin-5-yl)-1-(R)-benzyloxymethyl-2-oxo-ethyl)-isobutyramide;

2-amino-N-(1-(R)-(2,4-difluoro-benzyloxymethyl)-2-oxo-2-(3-oxo-3a-(R)-pyridin-2-ylmethyl)-2-(2,2,2-trifluoro-ethyl)-2,3,3a,4,6,7-hexahydro-pyrazolo-[4,3-c]pyridin-5-yl)-ethyl)-2-methyl-propionamide;

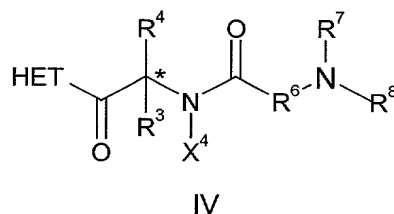
15

2-amino-N-{1(R)-benzyloxymethyl-2-[1,3-dioxo-8a(S)-pyridin-2-ylmethyl-2-(2,2,2-trifluoro-ethyl)-hexahydro-imidazo[1,5-a]pyrazin-7-yl]-2-oxo-ethyl}-2-methyl-propionamide;

20 N-(1(R)-((1,2-dihydro-1-methanesulfonyl-spiro(3H-indole-3,4'-piperidin)-1'-yl)carbonyl)-2-(phenylmethoxy)ethyl)-2-amino-2-methyl-propanamide; or

a prodrug of any of these compounds or a pharmaceutically acceptable salt of any of said compounds or said prodrugs.

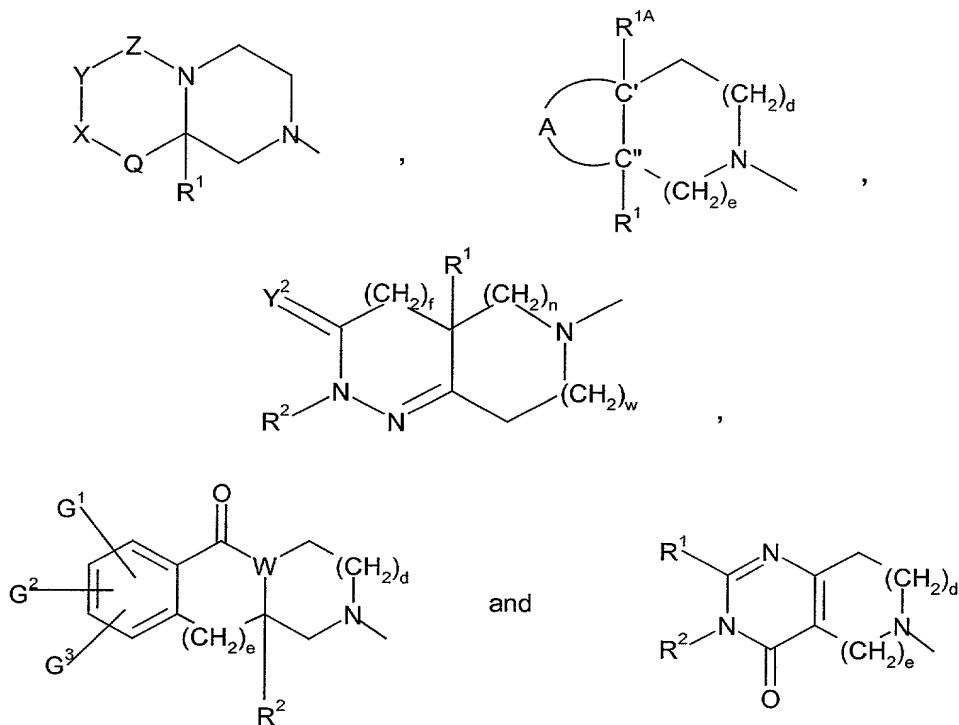
25 17. A pharmaceutical composition according to claim 13 wherein said growth hormone secretagogue is a compound of formula IV:



30 or a stereoisomeric mixture thereof, a diastereomerically enriched, diastereomerically pure, enantiomerically enriched, or enantiomerically pure isomer thereof, or a prodrug

of such compound, mixture, or isomer thereof, or a pharmaceutically acceptable salt of the compound, mixture, isomer, or prodrug, wherein:

HET is a heterocyclic moiety selected from the group consisting of



5 d is 0, 1, or 2;

e is 1 or 2;

f is 0 or 1;

n and w are 0, 1, or 2, provided that n and w cannot both be 0 at the same time;

10 Y² is oxygen or sulfur;

A is a divalent radical, wherein the left hand side of the radical as shown below is connected to C'' and the right hand side of the radical as shown below is connected to C', selected from the group consisting of -NR²-CO-NR²-, -NR²-SO₂-NR²-, -O-CO-NR²-, -NR²-CO₂-, -CO-NR²-CO-, -CO-NR²-C(R⁹R¹⁰)-, -C(R⁹R¹⁰)-NR²-CO-, -C(R⁹R¹⁰)-C(R⁹R¹⁰)-C(R⁹R¹⁰)-, -SO₂-C(R⁹R¹⁰)-C(R⁹R¹⁰)-, -C(R⁹R¹⁰)-O-CO-, -C(R⁹R¹⁰)-O-C(R⁹R¹⁰)-, -NR²-CO-C(R⁹R¹⁰)-, -O-CO-C(R⁹R¹⁰)-, -C(R⁹R¹⁰)-CO-NR²-, -CO-NR²-CO-, -C(R⁹R¹⁰)-CO₂-, -CO-NR²-C(R⁹R¹⁰)-C(R⁹R¹⁰)-, -CO₂-C(R⁹R¹⁰)-, -C(R⁹R¹⁰)-C(R⁹R¹⁰)-C(R⁹R¹⁰)-C(R⁹R¹⁰)-, -SO₂-NR²-C(R⁹R¹⁰)-C(R⁹R¹⁰)-, -C(R⁹R¹⁰)-C(R⁹R¹⁰)-NR²-CO-, -C(R⁹R¹⁰)-C(R⁹R¹⁰)-O-CO-, -NR²-CO-

$C(R^9R^{10})-C(R^9R^{10})-$, $-NR^2-SO_2-C(R^9R^{10})-C(R^9R^{10})-$, $-O-CO-C(R^9R^{10})-C(R^9R^{10})-$,
 $-C(R^9R^{10})-C(R^9R^{10})-CO-NR^2-$, $-C(R^9R^{10})-C(R^9R^{10})-CO-$, $-C(R^9R^{10})-NR^2-CO_2-$,
 $-C(R^9R^{10})-O-CO-NR^2$, $-C(R^9R^{10})-NR^2-CO-NR^2-$, $-NR^2-CO_2-C(R^9R^{10})-$, $-NR^2-CO-NR^2-$
 $C(R^9R^{10})-$, $-NR^2-SO_2-NR^2-C(R^9R^{10})-$, $-O-CO-NR^2-C(R^9R^{10})-$, $-CO-N=C(R^{11})-NR^2-$,
5 $-CO-NR^2-C(R^{11})=N-$, $-C(R^9R^{10})-NR^{12}-C(R^9R^{10})-$, $-NR^{12}-C(R^9R^{10})-$, $-NR^{12}-C(R^9R^{10})-$
 $C(R^9R^{10})-$, $-CO_2-C(R^9R^{10})-C(R^9R^{10})-$, $-NR^2-C(R^{11})=N-CO-$, $-C(R^9R^{10})-C(R^9R^{10})-N(R^{12})-$,
 $-C(R^9R^{10})-NR^{12}-$, $-N=C(R^{11})-NR^2-CO-$, $-C(R^9R^{10})-C(R^9R^{10})-NR^2-SO_2-$, $-C(R^9R^{10})-$
 $C(R^9R^{10})-SO_2-NR^2-$, $-C(R^9R^{10})-C(R^9R^{10})-CO_2-$, $-C(R^9R^{10})-SO_2-C(R^9R^{10})-$, $-C(R^9R^{10})-$
 $C(R^9R^{10})-SO_2-$, $-O-C(R^9R^{10})-C(R^9R^{10})-$, $-C(R^9R^{10})-C(R^9R^{10})-O-$, $-C(R^9R^{10})-CO-$
10 $C(R^9R^{10})-$, $-CO-C(R^9R^{10})-C(R^9R^{10})-$, and $-C(R^9R^{10})-NR^2-SO_2-NR^2-$;

Q is a covalent bond or CH_2 ;

W is CH or N;

X is CR^9R^{10} , $C=CH_2$, or $C=O$;

Y is CR^9R^{10} , O, or NR^2 ;

15 Z is $C=O$, $C=S$, or SO_2 ;

G^1 is hydrogen, halo, hydroxy, nitro, amino, cyano, phenyl, carboxyl, $-CONH_2$,
 $-C_1-C_4$ alkyl optionally independently substituted with one or more phenyl, one or
more halogen, or one or more hydroxy groups, $-C_1-C_4$ alkoxy optionally independently
substituted with one or more phenyl, one or more halogen, or one or more hydroxy
20 groups, $-C_1-C_4$ alkylthio, phenoxy, $-CO_2-(C_1-C_4$ alkyl), N,N-di- $(C_1-C_4$ alkylamino), $-C_2-$
 C_6 alkenyl optionally independently substituted with one or more phenyl, one or more
halogen, or one or more hydroxy groups, $-C_2-C_6$ alkynyl optionally independently
substituted with one or more phenyl, one or more halogen, or one or more hydroxy
groups, $-C_3-C_6$ cycloalkyl optionally independently substituted with one or more C_1-C_4
25 alkyl groups, one or more halogen, or one or more hydroxy groups, $-C_1-C_4$ alkylamino
carbonyl, or di- C_1-C_4 alkylamino) carbonyl;

G^2 and G^3 are each independently selected from the group consisting of
hydrogen, halo, hydroxy, $-C_1-C_4$ alkyl optionally independently substituted with one to
three halo groups, and $-C_1-C_4$ alkoxy optionally independently substituted with one to
30 three halo groups;

R^1 is hydrogen, $-CN$, $-(CH_2)_qNX^6COX^6$, $-(CH_2)_qNX^6CO(CH_2)_tA^1$,
 $-(CH_2)_qNX^6SO_2(CH_2)_tA^1$, $-(CH_2)_qNX^6SO_2X^6$, $-(CH_2)_qNX^6CONX^6(CH_2)_tA^1$,
 $-(CH_2)_qNX^6CONX^6X^6$, $-(CH_2)_qCONX^6X^6$, $-(CH_2)_qCONX^6(CH_2)_tA^1$, $-(CH_2)_qCO_2X^6$,
 $-(CH_2)_qCO_2(CH_2)_tA^1$, $-(CH_2)_qOX^6$, $-(CH_2)_qOCOX^6$, $-(CH_2)_qOCO(CH_2)_tA^1$,

$-(CH_2)_qOCONX^6(CH_2)_tA^1$, $-(CH_2)_qOCONX^6X^6$, $-(CH_2)_qCOX^6$, $-(CH_2)_qCO(CH_2)_tA^1$,
 $-(CH_2)_qNX^6CO_2X^6$, $-(CH_2)_qNX^6SO_2NX^6X^6$, $-(CH_2)_qSO_mX^6$, $-(CH_2)_qSO_m(CH_2)_tA^1$,
 $-C_1-C_{10}$ alkyl, $-(CH_2)_tA^1$, $-(CH_2)_q-(C_3-C_7$ cycloalkyl), $-(CH_2)_q-Y^1-(C_1-C_6$ alkyl), $-(CH_2)_q-$
 $Y^1-(CH_2)_tA^1$, or $-(CH_2)_q-Y^1-(CH_2)_t-(C_3-C_7$ cycloalkyl);

5 wherein the alkyl and cycloalkyl groups in the definition of R^1 are optionally substituted with C_1-C_4 alkyl, hydroxy, C_1-C_4 alkoxy, carboxyl, $-CONH_2$, $-SO_m-(C_1-C_6$ alkyl), $-CO_2-(C_1-C_4$ alkyl) ester, 1H-tetrazol-5-yl, or 1, 2, or 3 fluoro groups;

10 Y^1 is O, SO_m , $-CONX^6$, $-CH=CH-$, $-C\equiv C-$, $-NX^6CO-$, $-CONX^6$, $-CO_2-$, $-OCONX^6$ or $-OCO-$;

q is 0, 1, 2, 3, or 4;

t is 0, 1, 2, or 3;

15 said $(CH_2)_q$ group and $(CH_2)_t$ group in the definition of R^1 are optionally independently substituted with hydroxy, C_1-C_4 alkoxy, carboxyl, $-CONH_2$, $-SO_m-(C_1-C_6$ alkyl), $-CO_2-(C_1-C_4$ alkyl) ester, 1H-tetrazol-5-yl, 1, 2, or 3 fluoro groups, or 1 or 2 C_1-C_4 alkyl groups;

R^{1A} is selected from the group consisting of hydrogen, F, Cl, Br, I, C_1-C_6 alkyl, phenyl- $(C_1-C_3$ alkyl), pyridyl- $(C_1-C_3$ alkyl), thiazolyl- $(C_1-C_3$ alkyl), and thienyl- $(C_1-C_3$ alkyl), provided that R^{1A} is not F, Cl, Br, or I when a heteroatom is vicinal to C";

20 R^2 is hydrogen, C_1-C_8 alkyl, $-(C_0-C_3$ alkyl)- $(C_3-C_8$ cycloalkyl), $-(C_1-C_4$ alkyl)- A^1 , or A^1 , wherein the alkyl groups and the cycloalkyl groups in the definition of R^2 are optionally substituted with hydroxy, $-CO_2X^6$, $-CONX^6X^6$, $-NX^6X^6$, $-SO_m(C_1-C_6$ alkyl), $-COA^1$, $-COX^6$, CF_3 , CN, or 1, 2, or 3 independently selected halo groups;

25 R^3 is selected from the group consisting of A^1 , C_1-C_{10} alkyl, $-(C_1-C_6$ alkyl)- A^1 , $-(C_1-C_6$ alkyl)- $(C_3-C_7$ cycloalkyl), $-(C_1-C_5$ alkyl)- $X^1-(C_1-C_5$ alkyl), $-(C_1-C_5$ alkyl)- $X^1-(C_0-C_5$ alkyl)- A^1 , and $-(C_1-C_5$ alkyl)- $X^1-(C_1-C_5$ alkyl)- $(C_3-C_7$ cycloalkyl);

wherein the alkyl groups in the definition of R^3 are optionally substituted with $-SO_m(C_1-C_6$ alkyl), $-CO_2X^3$, 1, 2, 3, 4, or 5 independently selected halo groups, or 1, 2, or 3 independently selected $-OX^3$ groups;

30 X^1 is O, SO_m , $-NX^2CO-$, $-CONX^2$, $-OCO-$, $-CO_2-$, $-CX^2=CX^2-$, $-NX^2CO_2-$, $-OCONX^2$, or $-C\equiv C-$;

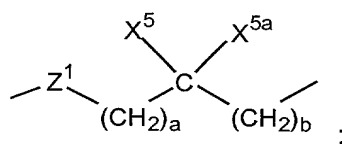
R^4 is hydrogen, C_1-C_6 alkyl, or C_3-C_7 cycloalkyl, or R^4 taken together with R^3 and the carbon atom to which they are attached form C_5-C_7 cycloalkyl, C_5-C_7 cycloalkenyl, a partially saturated or fully saturated 4- to 8-membered ring having 1 to

4 heteroatoms independently selected from the group consisting of oxygen, sulfur, and nitrogen, or a bicyclic ring system consisting of a partially saturated or fully saturated 5- or 6-membered ring, fused to a partially saturated, fully unsaturated, or fully saturated 5- or 6-membered ring, optionally having 1 to 4 heteroatoms

5 independently selected from the group consisting of nitrogen, sulfur, and oxygen;

X^4 is hydrogen or C_1 - C_6 alkyl, or X^4 is taken together with R^4 and the nitrogen atom to which X^4 is attached and the carbon atom to which R^4 is attached and form a five to seven membered ring;

R^6 is a bond or is



wherein a and b are each independently 0, 1, 2, or 3;

X^5 and X^{5a} are each independently selected from the group consisting of hydrogen, CF_3 , A^1 , and C_1 - C_6 alkyl optionally substituted with A^1 , OX^2 , -
15 SO_m -(C_1 - C_6 alkyl), $-CO_2X^2$, C_3 - C_7 cycloalkyl, $-NX^2X^2$, or $-CONX^2X^2$;

or the carbon bearing X^5 or X^{5a} forms one or two alkylene bridges with the nitrogen atom bearing R^7 and R^8 wherein each alkylene bridge contains 1 to 5 carbon atoms, provided that when one alkylene bridge is formed then only one of X^5 or X^{5a} is on the carbon atom and only one of R^7 or R^8 is on the
20 nitrogen atom, and further provided that when two alkylene bridges are formed then X^5 and X^{5a} cannot be on the carbon atom and R^7 and R^8 cannot be on the nitrogen atom;

or X^5 taken together with X^{5a} and the carbon atom to which they are attached form a partially saturated or fully saturated 3- to 7-membered ring, or
25 a partially saturated or fully saturated 4- to 8-membered ring having 1 to 4 heteroatoms independently selected from the group consisting of oxygen, sulfur, and nitrogen;

or X^5 taken together with X^{5a} and the carbon atom to which they are attached form a bicyclic ring system consisting of a partially saturated or fully
30 saturated 5- or 6-membered ring, optionally having 1 or 2 heteroatoms independently selected from the group consisting of nitrogen, sulfur, and

oxygen, fused to a partially saturated, fully saturated, or fully unsaturated 5- or 6-membered ring, optionally having 1 to 4 heteroatoms independently selected from the group consisting of nitrogen, sulfur, and oxygen;

Z^1 is a bond, O, or $N-X^2$, provided that when a and b are both 0 then

5 Z^1 is not $N-X^2$ or O;

R^7 and R^8 are each independently hydrogen or C_1 - C_6 alkyl optionally independently substituted with A^1 , $-CO_2$ -(C_1 - C_6 alkyl), $-SO_m$ -(C_1 - C_6 alkyl), 1 to 5 halo groups, 1 to 3 hydroxy groups, 1 to 3 $-O-CO$ -(C_1 - C_{10} alkyl) groups, or 1 to 3 C_1 - C_6 alkoxy groups; or

10 R^7 and R^8 can be taken together to form $-(CH_2)_r-L-(CH_2)_r-$, wherein L is CX^2X^2 , SO_m , or NX^2 ;

R^9 and R^{10} are each independently selected from the group consisting of hydrogen, fluoro, hydroxy, and C_1 - C_5 alkyl optionally independently substituted with 1-5 halo groups;

15 R^{11} is selected from the group consisting of C_1 - C_5 alkyl and phenyl optionally substituted with 1-3 substituents each independently selected from the group consisting of C_1 - C_5 alkyl, halo, and C_1 - C_5 alkoxy;

R^{12} is selected from the group consisting of C_1 - C_5 alkylsulfonyl, C_1 - C_5 alkanoyl, and C_1 - C_5 alkyl wherein the alkyl portion is optionally independently substituted by 1-5 halo groups;

20 A^1 for each occurrence is independently selected from the group consisting of C_5 - C_7 cycloalkenyl, phenyl, a partially saturated, fully saturated, or fully unsaturated 4- to 8-membered ring optionally having 1 to 4 heteroatoms independently selected from the group consisting of oxygen, sulfur, and nitrogen, and a bicyclic ring system consisting of a partially saturated, fully unsaturated, or fully saturated 5- or 6-membered ring, optionally having 1 to 4 heteroatoms independently selected from the group consisting of nitrogen, sulfur, and oxygen, fused to a partially saturated, fully saturated, or fully unsaturated 5- or 6-membered ring, optionally having 1 to 4 heteroatoms independently selected from the group consisting of nitrogen, sulfur, and oxygen;

30 A^1 for each occurrence is independently optionally substituted, on one or optionally both rings if A^1 is a bicyclic ring system, with up to three substituents, each substituent independently selected from the group consisting of F, Cl, Br, I, OCF_3 , OCF_2H , CF_3 , CH_3 , OCH_3 , $-OX^6$, $-CONX^6X^6$, -

CO₂X⁶, oxo, C₁-C₆ alkyl, nitro, cyano, benzyl, -SO_m(C₁-C₆ alkyl), 1H-tetrazol-5-yl, phenyl, phenoxy, phenylalkyloxy, halophenyl, methylenedioxy, -NX⁶X⁶, -NX⁶COX⁶, -SO₂NX⁶X⁶, -NX⁶SO₂-phenyl, NX⁶SO₂X⁶, -CONX¹¹X¹², -SO₂NX¹¹X¹², -NX⁶SO₂X¹², -NX⁶CONX¹¹X¹², -NX⁶SO₂NX¹¹X¹², -NX⁶COX¹²,
 5 imidazolyl, thiazolyl, and tetrazolyl, provided that if A¹ is optionally substituted with methylenedioxy then it can only be substituted with one methylenedioxy;

wherein X¹¹ is hydrogen or C₁-C₆ alkyl optionally independently substituted with phenyl, phenoxy, C₁-C₆ alkoxy carbonyl, -SO_m(C₁-C₆ alkyl), 1 to 5 halo groups, 1 to 3 hydroxy groups, 1 to 3 C₁-C₁₀ alkanoyloxy groups, or 1 to 3 C₁-C₆ alkoxy groups;

10 X¹² is hydrogen, C₁-C₆ alkyl, phenyl, thiazolyl, imidazolyl, furyl, or thienyl, provided that when X¹² is not hydrogen, the X¹² group is optionally substituted with one to three substituents independently selected from the group consisting of Cl, F, CH₃, OCH₃, OCF₃, and CF₃;

15 or X¹¹ and X¹² are taken together to form -(CH₂)_r-L¹-(CH₂)_r, wherein L¹ is CX²X², O, SO_m, or NX²;

r for each occurrence is independently 1, 2, or 3;

20 X² for each occurrence is independently hydrogen, optionally substituted C₁-C₆ alkyl, or optionally substituted C₃-C₇ cycloalkyl, wherein the optionally substituted C₁-C₆ alkyl and optionally substituted C₃-C₇ cycloalkyl in the definition of X² are optionally independently substituted with -SO_m(C₁-C₆ alkyl), -CO₂X³, 1 to 5 halo groups, or 1-3 OX³ groups;

X³ for each occurrence is independently hydrogen or C₁-C₆ alkyl;

25 X⁶ for each occurrence is independently hydrogen, optionally substituted C₁-C₆ alkyl, halogenated C₂-C₆ alkyl, optionally substituted C₃-C₇ cycloalkyl, halogenated C₃-C₇ cycloalkyl, wherein the optionally substituted C₁-C₆ alkyl and optionally substituted C₃-C₇ cycloalkyl in the definition of X⁶ are optionally independently mono- or di-substituted with C₁-C₄ alkyl, hydroxy, C₁-C₄ alkoxy, carboxyl, CONH₂, -SO_m(C₁-C₆ alkyl), carboxylate (C₁-C₄ alkyl) ester, or 1H-tetrazol-5-yl; or

30 when there are two X⁶ groups on one atom and both X⁶ are independently C₁-C₆ alkyl, the two C₁-C₆ alkyl groups may be optionally joined, and together with the atom to which the two X⁶ groups are attached, form a 4- to 9- membered ring

optionally having oxygen, sulfur, or NX^7 as a ring member, wherein X^7 is hydrogen or $\text{C}_1\text{-C}_6$ alkyl optionally substituted with hydroxy;

m for each occurrence is independently 0, 1, or 2;

with the provisos that:

- 5 X^6 and X^{12} cannot be hydrogen when attached to CO or SO_2 in the form COX^6 , COX^{12} , SO_2X^6 or SO_2X^{12} ; and

when R^6 is a bond then L is NX^2 and each r in the definition $-(\text{CH}_2)_r\text{-L-(CH}_2)_r\text{-}$ is independently 2 or 3.

- 10 18. A pharmaceutical composition according to claim 17 wherein said growth hormone secretagogue is

2-amino-N-(2-(3a(R)-benzyl-2-methyl-3-oxo-2,3,3a,4,6,7-hexahydro-pyrazolo-[4,3-c]pyridin-5-yl)-1-(R)-benzyloxymethyl-2-oxo-ethyl)-isobutyramide;

- 15 2-amino-N-(1-(R)-(2,4-difluoro-benzyloxymethyl)-2-oxo-2-(3-oxo-3a-(R)-pyridin-2-ylmethyl)-2-(2,2,2-trifluoro-ethyl)-2,3,3a,4,6,7-hexahydro-pyrazolo-[4,3-c]pyridin-5-yl)-ethyl)-2-methyl-propionamide;

- 20 2-amino-N-{1(R)-benzyloxymethyl-2-[1,3-dioxo-8a(S)-pyridin-2-ylmethyl-2-(2,2,2-trifluoro-ethyl)-hexahydro-imidazo[1,5-a]pyrazin-7-yl]-2-oxo-ethyl}-2-methyl-propionamide;

N-(1(R)-((1,2-dihydro-1-methanesulfonyl-spiro(3H-indole-3,4'-piperidin)-1'-yl)carbonyl)-2-(phenylmethoxy)ethyl)-2-amino-2-methyl-propanamide; or

- 25 a prodrug of any of these compounds, or a pharmaceutically acceptable salt of any of these compounds or prodrugs.

19. A pharmaceutical composition according to claim 18 wherein said corticotropin releasing factor antagonist is 4-(1-ethyl-propoxy)-3,6-dimethyl-2-(2,4,6-trimethylphenoxy)-pyridine and said growth hormone secretagogue is 2-amino-N-[2-(3a(R)-benzyl-2-methyl-3-oxo-2,3,3a,4,6,7-hexahydro-pyrazolo-[4,3-c]pyridin-5-yl)-1(R)-benzyloxymethyl-2-oxo-ethyl]-isobutyramide.
- 30

20. A pharmaceutical composition according to claim 18 wherein said corticotropin releasing factor antagonist is 4-(1-ethyl-propoxy)-3,6-dimethyl-2-(2,4,6-

trimethylphenoxy)-pyridine and said growth hormone secretagogue is 2-amino-N-(1(R)-(2,4-difluoro-benzyloxymethyl)-2-oxo-2-(3-oxo-3a(R)-(pyridin-2-ylmethyl)-2-(2,2,2-trifluoro-ethyl)-2,3,3a,4,6,7-hexahydro-pyrazolo-[4,3-c]pyridin-5-yl)-ethyl)-2-methyl-propionamide.

5

21. A pharmaceutical composition according to claim 18 wherein said corticotropin releasing factor antagonist is (3,6-dimethyl-2-(2,4,6-trimethyl-phenoxy)-pyridin-4-yl)-(1-ethyl-propyl)-amine and said growth hormone secretagogue is 2-amino-N-[2-(3a(R)-benzyl-2-methyl-3-oxo-2,3,3a,4,6,7-hexahydro-pyrazolo-[4,3-c]pyridin-5-yl)-1(R)-benzyloxymethyl-2-oxo-ethyl]-isobutyramide.

10

22. A pharmaceutical composition according to claim 18 wherein said corticotropin releasing factor antagonist is (3,6-dimethyl-2-(2,4,6-trimethyl-phenoxy)-pyridin-4-yl)-(1-ethyl-propyl)-amine and said growth hormone secretagogue is 2-amino-N-(1(R)-(2,4-difluoro-benzyloxymethyl)-2-oxo-2-(3-oxo-3a(R)-(pyridin-2-ylmethyl)-2-(2,2,2-trifluoro-ethyl)-2,3,3a,4,6,7-hexahydro-pyrazolo-[4,3-c]pyridin-5-yl)-ethyl)-2-methyl-propionamide.

15

23. A method for treating or preventing osteoporosis or frailty associated with aging or obesity, said method comprising administering to a human or other animal an amount of a pharmaceutical composition according to claim 1, which is effective in treating or preventing osteoporosis or frailty associated with aging or obesity.

20

24. A method for treating or preventing a cardiovascular or heart related disease, said method comprising administering to a human or other animal an amount of a pharmaceutical composition according to claim 1, which is effective in treating or preventing the cardiovascular or heart related disease.

25

25. A method according to claim 24 wherein the cardiovascular or heart related disease is hypertension, tachycardia, or congestive heart failure.

30

26. A method for accelerating bone fracture repair, attenuating protein catabolic response after a major operation, reducing cachexia and protein loss due to

chronic illness, accelerating wound healing, or accelerating the recovery of burn patients or of patients having undergone major surgery, said method comprising administering to a human or other animal an amount of a pharmaceutical composition according to claim 1, which is effective in accelerating bone fracture repair,
5 attenuating protein catabolic response after a major operation, reducing cachexia and protein loss due to chronic illness, accelerating wound healing, or accelerating the recovery of burn patients or of patients having undergone major surgery.

27. A method for treating or preventing osteoporosis, frailty associated
10 with aging or obesity, cardiovascular or heart related disease, for accelerating bone fracture repair, attenuating protein catabolic response after a major operation, reducing cachexia and protein loss due to chronic illness, accelerating wound healing, or accelerating the recovery of burn patients or of patients having undergone major surgery, said method comprising administering to a human or other animal an
15 amount of a corticotropin releasing factor antagonist and an amount of a growth hormone secretagogue or growth hormone.

28. The method of claim 27 wherein said corticotropin releasing factor antagonist and said growth hormone secretagogue or growth hormone are
20 administered simultaneously or in a specifically timed manner.

29. A kit comprising:
a. an amount of a corticotropin releasing factor antagonist, in a first unit dosage form;
25 b. an amount of a growth hormone secretagogue or growth hormone, in a second unit dosage form; and
c. a container.

30. A kit comprising:
a. an amount of a corticotropin releasing factor antagonist as defined in claim 13, in a first unit dosage form;
b. an amount of a growth hormone secretagogue or growth hormone, in a second unit dosage form; and
c. a container.

31. A kit comprising:
- a. an amount of a corticotropin releasing factor antagonist as defined in claim 14, in a first unit dosage form;
 - 5 b. an amount of a growth hormone secretagogue or growth hormone, in a second unit dosage form; and
 - c. a container.
32. A kit comprising:
- 10 a. an amount of a corticotropin releasing factor antagonist, in a first unit dosage form;
 - b. an amount of a growth hormone secretagogue as defined in claim 15, in a second unit dosage form; and
 - c. a container.
- 15 33. A kit according to claim 29 wherein said corticotropin releasing factor antagonist is 4-(1-ethyl-propoxy)-3,6-dimethyl-2-(2,4,6-trimethylphenoxy)-pyridine or [3,6-dimethyl-2-(2,4,6-trimethyl-phenoxy)-pyridin-4-yl]-(1-ethyl-propyl)-amine, and said growth hormone secretagogue is 2-amino-N-[2-(3a(R)-benzyl-2-methyl-3-oxo-2,3,3a,4,6,7-hexahydro-pyrazolo-[4,3-c]pyridin-5-yl)-1(R)-benzyloxymethyl-2-oxo-ethyl]-isobutyramide or 2-amino-N-(1-(R)-(2,4-difluoro-benzyloxymethyl)-2-oxo-2-(3-oxo-3a(R)-pyridin-2-ylmethyl)-2-(2,2,2-trifluoro-ethyl)-2,3,3a,4,6,7-hexahydro-pyrazolo-[4,3-c]pyridin-5-yl)-ethyl)-2-methyl-propionamide.
- 20 34. A kit, comprising
- 25 a. a pharmaceutical composition, comprising an amount of a growth hormone or growth hormone secretagogue;
 - b. a package containing the above composition; and
 - c. a package insert that may be integral with said package;
- 30 wherein it is stated on the package insert that the pharmaceutical composition is to be administered simultaneously or in a specifically timed manner with a pharmaceutical composition containing at least one corticotropin releasing factor antagonist.

35. A kit, comprising
 - a. a pharmaceutical composition, comprising an amount of a corticotropin releasing factor antagonist;
 - b. a package containing the above composition; and
 - c. a package insert that may be integral with said package;

wherein it is stated on the package insert that the pharmaceutical composition is to be administered simultaneously or in a specifically timed manner with a pharmaceutical composition containing at least one growth hormone or growth hormone secretagogue.